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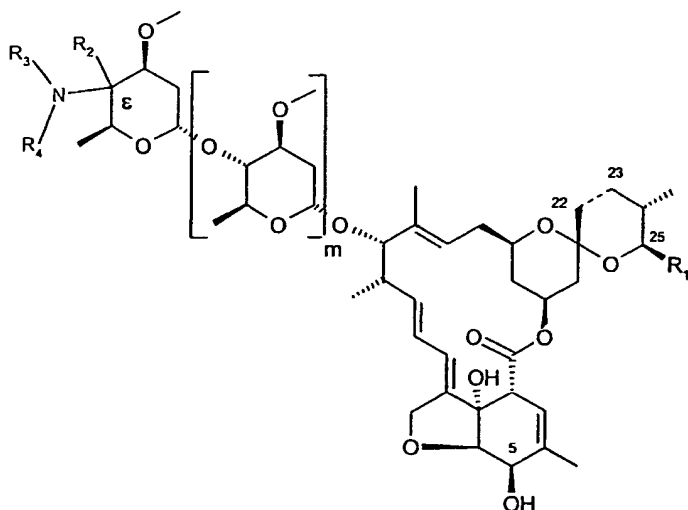
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(54) Title: AVERMECTIN AND AVERMECTIN MONOSACCHARIDE SUBSTITUTED IN THE 4'- AND 4'- POSITION RESPECTIVELY



(I)

(57) Abstract: A compound of the formula (I) wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond, m is 0 or 1, R<sub>1</sub> represents a C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl group, R<sub>2</sub> represents a hydrocarbyl group or a substituted hydrocarbyl group, and R<sub>3</sub> and R<sub>4</sub> represent, independently of each other, hydrogen or a chemical constituent, or either R<sub>2</sub> and R<sub>3</sub> together or R<sub>3</sub> and R<sub>4</sub> together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH<sub>2</sub> group may be replaced by O, S or NR<sub>6</sub> where R<sub>6</sub> represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer and/or tautomer of the compound of formula

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(I), in each case in free form or in salt form.



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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

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Avermectin and Avermectin monosaccharide substituted in the 4''- and 4'-position respectively

The present invention relates in particular to certain avermectin and avermectin monosaccharide derivatives, processes for preparing such derivatives, intermediates in the preparation of such derivatives, and the use of certain derivatives controlling pests.

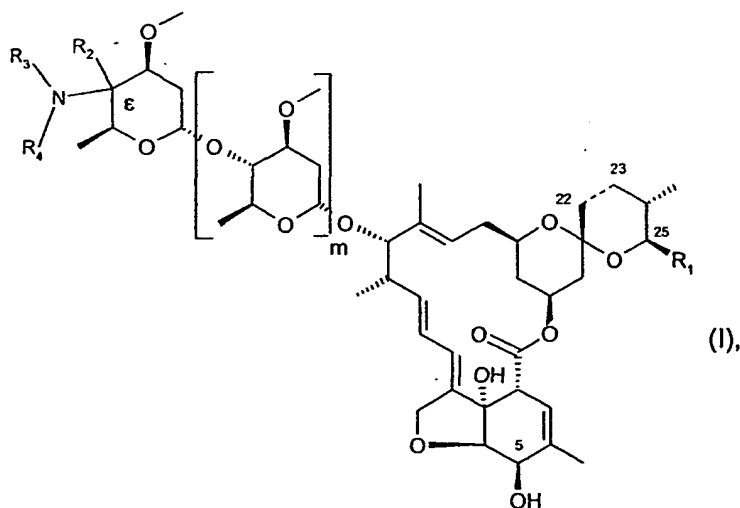
Certain macrolide compounds for controlling pests are known. However, the biological properties of these known compounds are not entirely satisfactory, and, as a consequence, there is still a need for providing further compounds having pesticidal properties.

10

It is found that certain desoxy derivatives of avermectin and avermectin monosaccharide, having a hydrocarbonyl group or substituted group thereof on the 4'' or 4' position, are useful in controlling pests, in particular pests that are harmful to crop plants and to its propagation material, such as representatives of the class insecta, the order Acarina and the class nematoda.

15

Accordingly, in a first aspect, the present invention provides a compound of the formula (I)



wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

m is 0 or 1,

5 R<sub>1</sub> represents a C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl group,

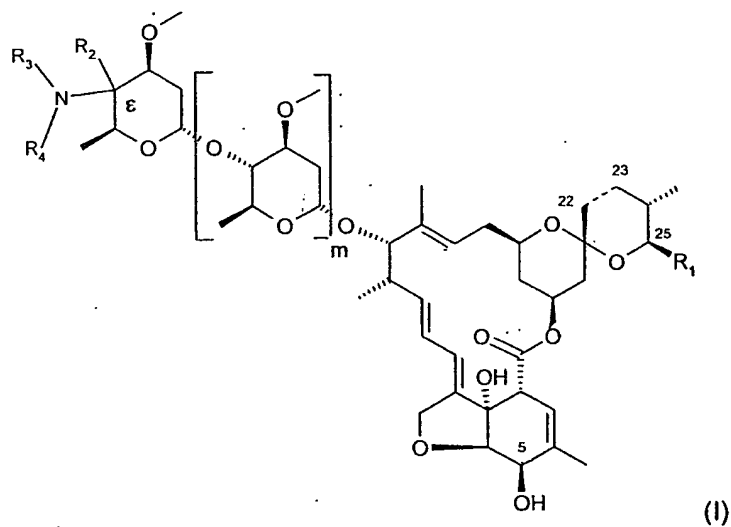
R<sub>2</sub> represents a hydrocarbyl group or a substituted hydrocarbyl group, and

10 R<sub>3</sub> and R<sub>4</sub> represent, independently of each other, hydrogen or a chemical constituent, or either R<sub>2</sub> and R<sub>3</sub> together or R<sub>3</sub> and R<sub>4</sub> together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH<sub>2</sub> group may be replaced by O, S<sup>+</sup> or NR<sub>6</sub>, where R<sub>6</sub> represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (I), in each case in free form or in salt form.

15 The symbol  $\epsilon$  represents that the configuration of the carbon atom at the 4'- or 4''-position is (S) or (R).

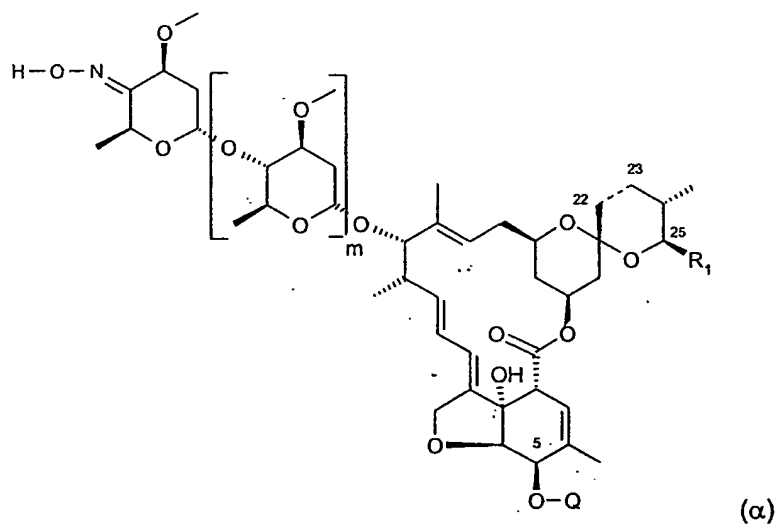
In a second aspect, the present invention provides a process for preparing a compound of formula (I)

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wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, comprising the steps of:

- 5 (i) synthesizing a compound of formula (α)



wherein R<sub>1</sub>, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in the first aspect and Q is a protecting group;

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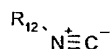
(ii) reacting a disulfide, an aliphatic or aromatic phosphine and a compound of formula ( $\alpha$ ) to yield a sulfenimine derivative of the compound of formula ( $\alpha$ );

(iii) oxidising the sulfenimine derivative of the compound of formula ( $\alpha$ ) to yield a sulfinimine derivative of the compound of formula ( $\alpha$ );

either

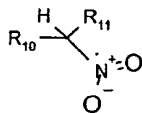
(iva) reacting an organometallic reagent having the  $R_2$  group with the sulfinimine derivative of the compound of formula ( $\alpha$ ) to yield a desoxy - sulfinamide - hydrocarbyl derivative of the compound of formula ( $\alpha$ ); or

10 (ivb) reacting an isocyanate reagent of formula



where  $R_{12}$  is unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or  
 15 mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl sulfone or unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl nitrile with the  
 20 sulfinimine derivative of the compound of formula ( $\alpha$ ) to yield a desoxy - amine - hydrocarbyl derivative of the compound of formula ( $\alpha$ ); or

(ivc) reacting an nitro alkyl reagent of formula



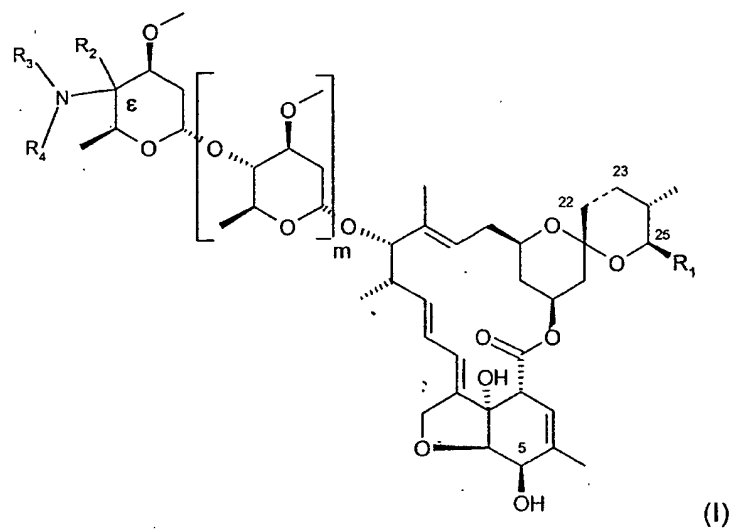
where  $R_{10}$  and  $R_{11}$  are independently of each other, H, CN, unsubstituted or mono- to  
 25 pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl,

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- unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkenyl, unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl sulfone or unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy- amine - hydrocarbyl derivative of the compound of formula (α); and
- either
- 10 (va) removing the sulfinyl group and protecting group Q either in one step or sequentially one after another to yield a compound of formula (I), where R<sub>3</sub> and R<sub>4</sub> each represent hydrogen, or
- (vb) removing the sulfinyl group alone, carrying out reactions on one or more of the R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> groups to modify the group and then removing the protecting group Q to yield a
- 15 compound of formula (I), or
- (vc) removing the protecting group Q if the sulfinyl group is removed during (iva) or (ivb) or (ivc) to yield a compound of formula (I).

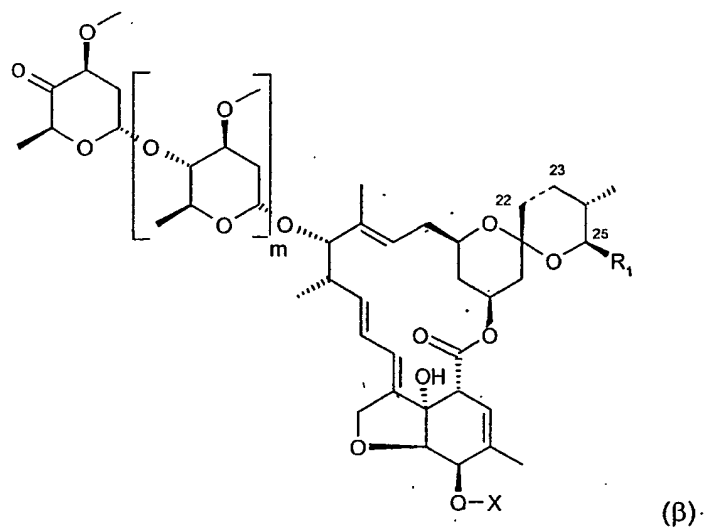
- In a third aspect, the present invention provides a process for preparing a compound of
- 20 formula (I)

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wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, the bond between the carbon atoms 22 and 23 and *m* are as  
 5 defined in the first aspect, comprising the steps of:

(i) synthesizing a compound of formula (β)





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wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  is as defined for formula (I) in the first aspect and  $X$  is H or Q, where Q is a protecting group;

- (ii) reacting N- $R_4$ hydroxylamine or salt thereof with a compound of formula ( $\beta$ ) to yield a  
5     nitron derivative of the compound of formula ( $\beta$ );

either

- (iiia) reacting an organometallic or a silyl reagent having the  $R_2$  group with nitron derivative  
of the compound of formula ( $\beta$ ) to yield a desoxy – N- $R_4$ hydroxylamino - hydrocarbyl  
10     derivative of the compound of formula ( $\beta$ ), where  $R_4$  is as defined for formula (I) of the first  
aspect, or

(iiib) reacting an alkene or an alkyne derivative with the nitron derivative of the compound  
of formula ( $\beta$ ) to yield a desoxy – N-isoxazolidine derivative or 2,3-dihydro-isoxazole  
derivative respectively of the compound of formula ( $\beta$ ); and

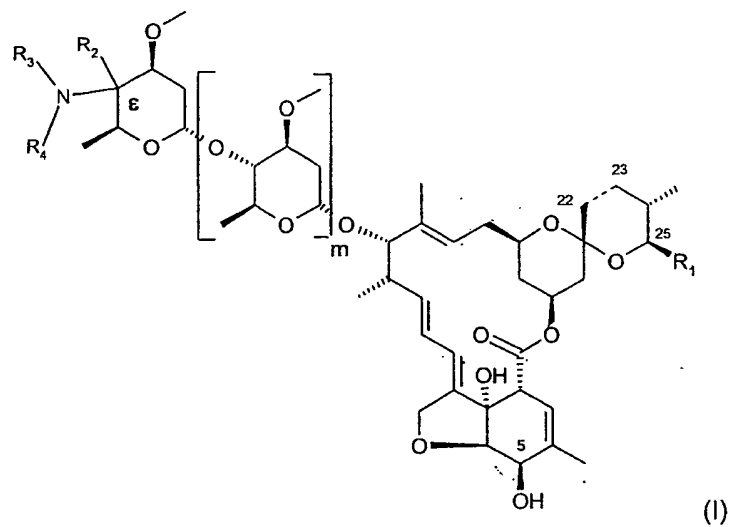
15

either

- (iva) removing the protecting group Q, if present, to yield a compound of formula (I), where  
 $R_3$  is OH in the event of reaction step (iiia), or where  $R_2$  and  $R_3$  is an alkylene or alkenylene  
bridge with a  $CH_2$  group replaced by an oxygen atom in the event of reaction step (iiib), or  
20     (ivb) carrying out reactions on one or more of  $R_2$ ,  $R_3$  and  $R_4$  groups to modify the group and  
removing the protecting group Q, if present, to yield a compound of formula (I).

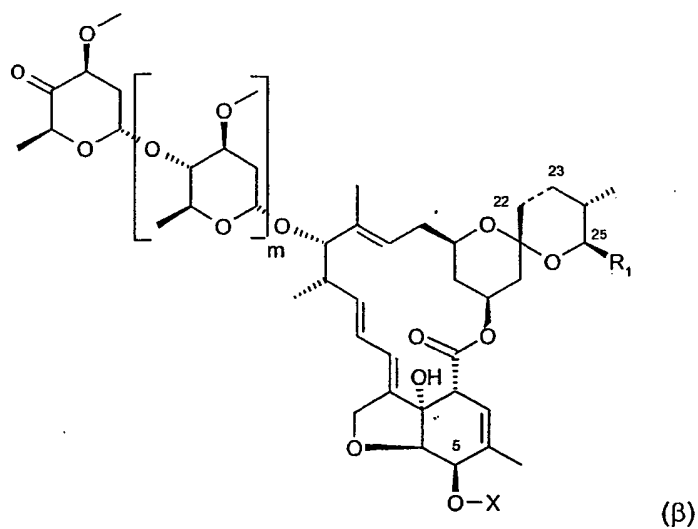
In a fourth aspect, the present invention provides a process for preparing a compound of  
formula (I)

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wherein  $R_1$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined for formula (I) in the first aspect and  $R_2$  is CN, comprising the steps of:

- 5 (i) synthesizing a compound of formula ( $\beta$ )



wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  is as defined in for formula (I) in the first aspect and  $X$  is H or Q, where Q is a protecting group;

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either

(iia) reacting the compound of formula ( $\beta$ ) with a silylated amine (having the  $R_3$  and  $R_4$  groups) in presence of a Lewis acid and a trialkylsilyl cyanide, to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula ( $\beta$ ), and wherein  $R_1$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, and  $R_2$  is CN, or

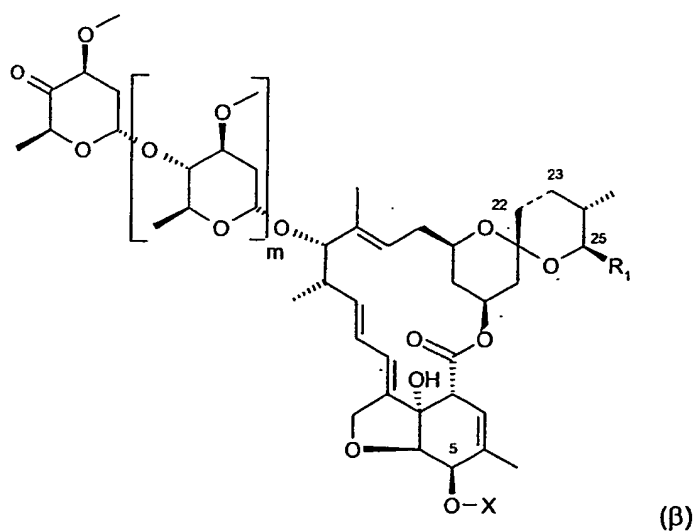
(iib) reacting the compound of formula ( $\beta$ ) with an amine of formula  $R_3R_4NH$ , a chlorosilane, a Lewis acid and a trialkylsilyl cyanide to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula ( $\beta$ ), and wherein  $R_1$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, and  $R_2$  is CN;

(iii) optionally carrying out reactions on one or both of  $R_3$  and  $R_4$  groups to modify the group; and

(iv) removing the protecting group Q, if present, to yield a compound of formula (I);

or

(i) synthesizing a compound of formula ( $\beta$ )



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wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined for formula (I) in the first aspect and  $X$  is H or Q, where Q is a protecting group;

- (ii) reacting the compound of formula ( $\beta$ ) with an ammonium salt of formula  $R_{18}CO_2NH_4^+$ ,  
5 an isocyanide of formula  $R_{12}NC$  to yield a compound of formula (I), with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula ( $\beta$ ), wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined in the first aspect,  $R_2$  is  $R_{12}NHC(O)$ , and  $R_4$  is  $R_{18}C(O)$ ,  $R_{18}$  is H, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  
10  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl sulfone or  
15 unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl nitrile and  $R_{12}$  is as defined in (ivb) of the second aspect; and

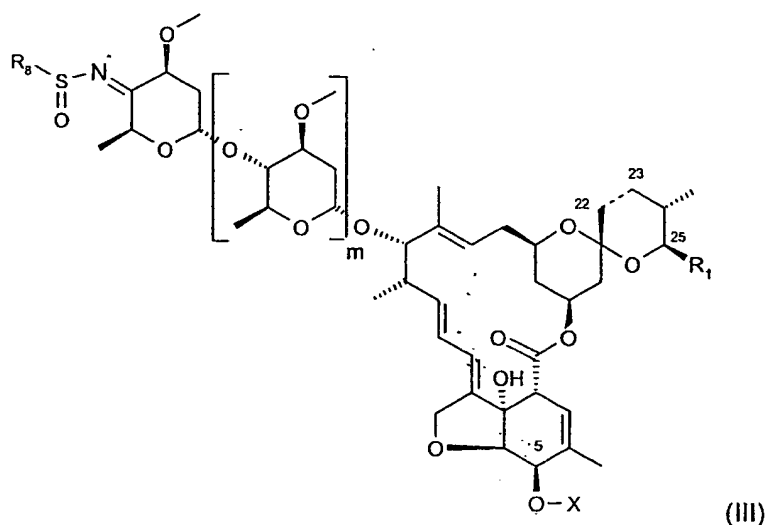
(iii) removing the protecting group Q, if present, to yield a compound of formula (I).

- 20 Generally, a preparation of a compound of formula (I) results in a mixture of compounds, so the present invention also extends to a mixture containing compounds of formula (I), such as a mixture containing E and Z isomers, *R* and *S* diastereoisomers, compounds with  $R_1$  is *i*Pr and compounds with  $R_1$  is *sec*-Bu or compounds of different tautomers, or a mixture thereof.

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In a fifth aspect, the present invention provides a compound of the formula (III)

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wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond;

$m$  is 0 or 1;

5  $R_1$  represents a  $C_1$ - $C_{12}$ alkyl,  $C_3$ - $C_8$ cycloalkyl or  $C_2$ - $C_{12}$ alkenyl, group;

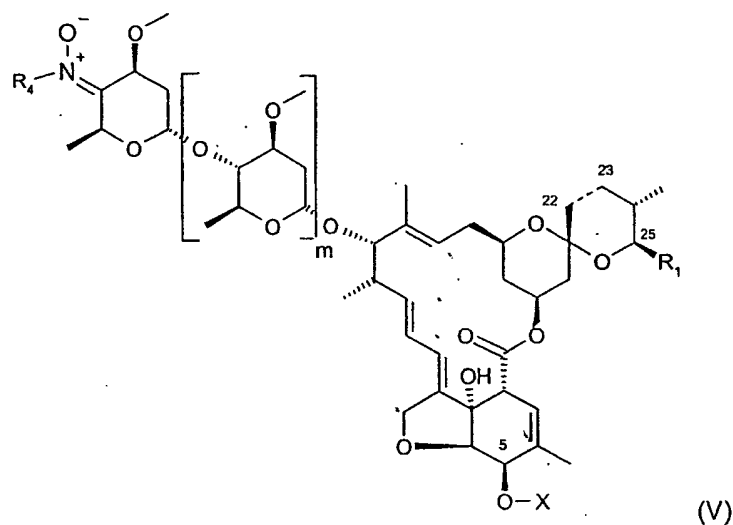
$R_8$  represents  $C_1$ - $C_6$ alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen,  $C_1$ - $C_6$ alkoxy, hydroxy, cyano, aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN,  $NO_2$ ,  $C_1$ - $C_{12}$ alkyl,  $C_1$ - $C_{12}$ haloalkyl,  $C_1$ - $C_{12}$ alkoxy,  $C_1$ - $C_{12}$ haloalkoxy,  $C_1$ - $C_{12}$ alkylthio and  $C_1$ - $C_{12}$ haloalkylthio, and

$X$  represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position.

or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (III), in each case in free form or in salt form.

In a sixth aspect, the present invention provides a compound of the formula (V)

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wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

$m$  is 0 or 1,

5  $R_1$  represents a  $C_1$ - $C_{12}$ alkyl,  $C_3$ - $C_8$ cycloalkyl or  $C_2$ - $C_{12}$ alkenyl, group,

$R_4$  represents a chemical constituent, and

$X$  represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (V), in each case in free form or in salt form.

In a seventh aspect, the present invention provides a pesticidal composition comprising at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, as active compound, and at least one auxiliary.

15

In an eighth aspect, the present invention provides a method for controlling pests comprising applying a composition defined in the seventh aspect to the pests or their habitat.

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In a ninth aspect, the present invention provides a process for preparing a composition defined in the seventh aspect comprising mixing intimately and/ or grinding at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, as active compound, with at least one auxiliary.

5

In a tenth aspect, the present invention provides the use of a compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, for preparing a composition as defined in the seventh aspect.

10

In an eleventh aspect, the present invention provides the use of a composition as defined in the seventh aspect for controlling pests.

15

In a twelfth aspect, the present invention provides a method for protecting plant propagation material comprising treating the propagation material, or the location where the propagation material is planted, with a composition defined in the seventh aspect.

20

In a thirteenth aspect, the present invention provides a pest resistant plant propagation material having adhered thereto at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively; preferably treated by the method of the twelfth aspect.

25

In a fourteenth aspect, the present invention provides the use of compound defined in the fifth or sixth aspect for preparing a compound of formula (I) as defined in the first aspect.

A compound of the present invention is a derivative of avermectin or avermectin monosaccharide.

Avermectins are known to the person skilled in the art. They are a group of structurally closely related pesticidally active compounds, which are obtained by fermenting a strain of the microorganism *Streptomyces avermitilis*. Also the derivatives where R<sub>1</sub> is not iso-propyl or sec-butyl, for example, it is cyclohexyl or 1-methyl butyl, are obtained by fermentation. Derivatives of Avermectins can be obtained by conventional chemical syntheses. The present invention relates to a new series of compounds having a hydrocarblyl group or substituted group thereof and an unsubstituted or substituted amine on the 4'' or 4' position of avermectin or avermectin monosaccharide respectively.

The avermectins, which can be obtained from *Streptomyces avermitilis*, are referred to as A1a, A1b, A2a, A2b, B1a, B1b, B2a and B2b. The compounds referred to as "A" and "B" have a methoxy radical and an OH group, respectively, in the 5-position. The "a" series and the "b" series are compounds in which the substituent R<sub>1</sub> (in position 25) is a sec-butyl radical and an isopropyl radical, respectively. The number 1 in the name of the compounds means that carbon atoms 22 and 23 are linked by a double bond; the number 2 means that they are linked by a single bond and that the carbon atom 23 carries an OH group. The above nomenclature is adhered to in the description of the present invention to denote the specific structure type in the not naturally occurring avermectin derivatives according to the invention, which corresponds to the naturally occurring avermectin. The compounds according to the invention are especially derivatives of avermectin compounds of the B1 series, advantageously B1a and B1b; derivatives having a single bond between carbon atoms 22 and 23; derivatives having substituents other than sec-butyl or isopropyl in position 25; and derivatives of the corresponding monosaccharides.

For a review of macrolide chemistries, see: Ivermectin and Abamectin. Fisher, M. H.; Mrozik, H. Editor(s) - Campbell, William Cecil, (1989), 1-23; and Macrolide Antibiotics (2nd Edition), Sunazuka, Toshiaki, Omura, Sadafumi; Iwasaki, Shigeo, Omura, Satoshi. Editor(s) - Omura, Satoshi (2002), 99-180.

Also the following articles describe synthetic routes to prepare monosaccharide avermectin derivatives: Mrozik, Helmut; Eskola, Philip; Arison, Byron H.; Albers-Schoenberg, George;



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Fisher, Michael H. *Journal of Organic Chemistry* (1982), 47(3), 489-92; and Bliard, Christophe; Escribano, Francisca Cabrera; Lukacs, Gabor; Olesker, Alain; Sarda, Pierre *Journal of the Chemical Society, Chemical Communications* (1987), 5), 368-70.

- 5 EP-A-0343708 further describes synthetic routes to prepare 4" or 4'-oxo and oxime avermectin derivatives.

Each compound of the invention may be present as a tautomer. Accordingly, the compound, for example, of formula (I) is, if appropriate, also to be understood as including  
10 the corresponding tautomer, even if the latter are not specifically mentioned in each case.

Each compound of the invention, such as compound of formula (I), and, where applicable, its tautomer can form salts, for example acid addition salts. These acid addition salts are formed, for example, with strong inorganic acids, such as mineral acids, for example,  
15 sulfuric acid, a phosphoric acid or a hydrohalic acid, with strong organic carboxylic acids, such as unsubstituted or substituted, for example halo-substituted, C<sub>1</sub>-C<sub>4</sub>alkanecarboxylic acids, for example, acetic acid, unsaturated or saturated dicarboxylic acids, for example, oxalic acid, malonic acid, maleic acid, fumaric acid or phthalic acid, hydroxycarboxylic acids, for example, ascorbic acid, lactic acid, malic acid, tartaric acid or citric acid, or  
20 benzoic acid, or with organic sulfonic acids, such as unsubstituted or substituted, for example, halo-substituted, C<sub>1</sub>-C<sub>4</sub>alkane- or aryl-sulfonic acids, for example, methane- or p-toluene-sulfonic acid. Compound of formula (I) that have at least one acidic group can furthermore form salts with bases. Suitable salts with bases are, for example, metal salts, such as alkali metal salts or alkaline earth metal salts, for example, sodium, potassium or  
25 magnesium salts, or salts with ammonia or with an organic amine, such as morpholine, piperidine, pyrrolidine, a mono-, di- or tri-lower alkylamine, for example, ethylamine, diethylamine, triethylamine or dimethylpropylamine, or a mono-, di- or trihydroxy-lower alkylamine, for example, mono-, di- or tri-ethanolamine. Corresponding internal salts may also be formed where appropriate. Among the salts of the compound of formula (I), the  
30 agrochemically advantageous salts are preferred.

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Any reference to the free compound of the invention, for example, of formula (I) or its salt, is to be understood as including, where appropriate, also the corresponding salt or the free compound of formula (I), respectively. The same applies to tautomer of compound of the invention, for example, of formula (I) and salt thereof.

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The invention is described in detail below. Further, as described below each embodiment of a feature of the present invention is independent of an embodiment of another feature.

In the context of the first aspect of the invention, preference is given to following groups:

- 10 (2) a compound of the first aspect (also referred to as group (1)) in free form (*i.e.*, not in salt form);
- (3) a compound of the first aspect (also referred to as group (1)) in salt form;
- 15 (4) a compound according to any one of groups (1) to (3), wherein  $R_2$  is unsubstituted  $C_1$ - $C_{12}$ alkyl or halogen-substituted  $C_1$ - $C_{12}$ alkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted  $C_3$ - $C_8$ cycloalkyl or halogen-substituted  $C_3$ - $C_8$ cycloalkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted  $C_2$ - $C_{12}$ alkenyl or halogen-substituted  $C_2$ - $C_{12}$ alkenyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted  $C_2$ - $C_8$ alkynyl or halogen-substituted  $C_2$ - $C_8$ alkynyl or in each case a mono- to pentasubstituted derivative thereof, CN, unsubstituted aryl or heterocyclyl, or aryl or heterocyclyl that are, depending on the possibilities of substitution on the ring, mono- to pentasubstituted by substituents selected from the group consisting of =O, OH, =S, SH, halogen, CN,  $NO_2$ ,  $C_1$ - $C_{12}$ alkyl,  $C_3$ - $C_8$ cycloalkyl,  $C_1$ - $C_{12}$ haloalkyl,  $C_1$ - $C_{12}$ alkoxy, 20  $C_1$ - $C_{12}$ haloalkoxy,  $C_1$ - $C_{12}$ alkylthio,  $C_1$ - $C_{12}$ haloalkylthio,  $C_1$ - $C_6$ alkoxy- $C_1$ - $C_6$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl, phenoxy and methylenedioxy;
- (5) a compound according to any one of groups (1) to (4), wherein  $R_3$  is hydrogen, unsubstituted  $C_1$ - $C_{12}$ alkyl or halogen-substituted  $C_1$ - $C_{12}$ alkyl or in each case a mono- to

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- pentasubstituted derivative thereof, unsubstituted C<sub>3</sub>-C<sub>8</sub>cycloalkyl or halogen-substituted C<sub>3</sub>-C<sub>8</sub>cycloalkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C<sub>2</sub>-C<sub>12</sub>alkenyl or halogen-substituted C<sub>2</sub>-C<sub>12</sub>alkenyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C<sub>2</sub>-C<sub>8</sub>alkynyl or halogen-substituted C<sub>2</sub>-C<sub>8</sub>alkynyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C<sub>1</sub>-C<sub>12</sub>alkoxy or halogen-substituted C<sub>1</sub>-C<sub>12</sub>alkoxy or in each case a mono- to pentasubstituted derivative thereof, unsubstituted or mono- to pentasubstituted phenoxy, OH, aryl, benzyl, heterocyclyl group, CN, -N(R<sub>5</sub>)<sub>2</sub>, -SR<sub>8</sub>, -S(=O)R<sub>8</sub>, -S(=O)<sub>2</sub>R<sub>8</sub>, or -S(=O)<sub>2</sub>N(R<sub>5</sub>)<sub>2</sub>;
- (6) a compound according to any one of groups (1) to (5), wherein R<sub>4</sub> is H, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl, unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkenyl, unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkynyl;
- (7) a compound according to any one of groups (1), (2), (3) and (6), wherein R<sub>2</sub> and R<sub>3</sub> together are a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a, CH<sub>2</sub> group may be replaced by O, S or NR<sub>6</sub>;
- (8) a compound according to any one of groups (1) to (4), wherein R<sub>3</sub> and R<sub>4</sub> together are a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a, CH<sub>2</sub> group may be replaced by O, S or NR<sub>6</sub>;
- The substituents of the alkyl, alkoxy, phenoxy, alkenyl, alkynyl, alkylene (whether CH<sub>2</sub> group replaced or not), alkenylene (whether CH<sub>2</sub> group replaced or not), cycloalkyl groups, and halogen substituted groups of alkyl, alkenyl, alkynyl and cycloalkyl, mentioned in any one of groups (1) to (8) are selected from the group consisting of OH, SH, =O, =S, halogen, CN, SCN, NO<sub>2</sub>, -N<sub>3</sub>, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl that is unsubstituted or substituted by one to three methyl groups, C<sub>3</sub>-C<sub>8</sub>cycloalkenyl that is unsubstituted or substituted by one to three methyl

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- groups, C<sub>3</sub>-C<sub>8</sub>halocycloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, halo-C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>2</sub>-C<sub>8</sub>alkenyloxy, C<sub>2</sub>-C<sub>8</sub>alkynyloxy, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>alkoxy-N(R<sub>5</sub>)<sub>2</sub> (wherein the two R<sub>5</sub> are independently of each other), C<sub>3</sub>-C<sub>8</sub>cycloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio, C<sub>1</sub>-C<sub>6</sub>alkylthio-C<sub>1</sub>-C<sub>6</sub>alkoxy, halo-C<sub>1</sub>-C<sub>12</sub>alkylthio, C<sub>3</sub>-C<sub>8</sub>cycloalkylthio, C<sub>3</sub>-C<sub>8</sub>heterocycloalkylthio, C<sub>1</sub>-C<sub>12</sub>alkylsulfinyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylsulfinyl, C<sub>1</sub>-C<sub>12</sub>haloalkylsulfinyl, C<sub>3</sub>-C<sub>8</sub>halocycloalkylsulfinyl, C<sub>1</sub>-C<sub>12</sub>alkylsulfonyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylsulfonyl, C<sub>1</sub>-C<sub>12</sub>haloalkylsulfonyl, C<sub>3</sub>-C<sub>8</sub>halocycloalkylsulfonyl, -N(R<sub>5</sub>)<sub>2</sub> (wherein the two R<sub>5</sub> are independently of each other or the two R<sub>5</sub> together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge), -C(=Y)OH, -C(=Y)R<sub>7</sub>, -X-C(=Y)R<sub>7</sub>, -P(=O)(OC<sub>1</sub>-C<sub>6</sub>alkyl)<sub>2</sub>, -S(=O)<sub>2</sub>R<sub>8</sub>, -NH-S(=O)<sub>2</sub>R<sub>8</sub>, -X-C(=O)-C<sub>1</sub>-C<sub>6</sub>alkyl-S(=O)<sub>2</sub>R<sub>8</sub>, aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio, heterocyclylthio, and aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio and heterocyclylthio, which, depending on the possibilities of substitution on the ring, are mono- to pentasubstituted by substituents selected from the group consisting of =O, OH, =S, SH, halogen, CN, NO<sub>2</sub>, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio, C<sub>1</sub>-C<sub>12</sub>haloalkylthio, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkyl, dimethylamino-C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, phenoxy, phenyl-C<sub>1</sub>-C<sub>6</sub>alkyl, methylenedioxy, -N(R<sub>5</sub>)<sub>2</sub> (wherein the two R<sub>5</sub> are independently of each other), -O-C(=O)-R<sub>7</sub>, -NH-C(=O)R<sub>7</sub>, -C(=O)R<sub>8</sub>, C<sub>1</sub>-C<sub>6</sub>alkylsulfinyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylsulfinyl, C<sub>1</sub>-C<sub>6</sub>haloalkylsulfinyl, C<sub>3</sub>-C<sub>8</sub>halocycloalkylsulfinyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, C<sub>3</sub>-C<sub>8</sub>cycloalkylsulfonyl, C<sub>1</sub>-C<sub>6</sub>haloalkylsulfonyl and C<sub>3</sub>-C<sub>8</sub>halocycloalkylsulfonyl;

where

- R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub>alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C<sub>3</sub>-C<sub>8</sub>-cycloalkoxy, hydroxy and cyano, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>3</sub>-C<sub>8</sub>-cycloalkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, aryl, benzyl, heteroaryl, or aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO<sub>2</sub>, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio and C<sub>1</sub>-C<sub>12</sub>haloalkylthio;

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R<sub>6</sub> represents H, C<sub>1</sub>-C<sub>8</sub>alkyl, hydroxy-C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, phenyl, benzyl, -C(=O)R<sub>9</sub> or -CH<sub>2</sub>-C(=O)R<sub>9</sub>;

5 R<sub>7</sub> represents H, C<sub>1</sub>-C<sub>24</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>hydroxyalkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>2</sub>-C<sub>8</sub>alkenyloxy, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkyl, N(R<sub>5</sub>)<sub>2</sub> (wherein the two R<sub>5</sub> are independently of each other), aryl, benzyl, heterocyclyl, or aryl, benzyl or heterocyclyl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group  
10 consisting of OH, halogen, CN, NO<sub>2</sub>, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio and C<sub>1</sub>-C<sub>12</sub>haloalkylthio;

R<sub>8</sub> represents C<sub>1</sub>-C<sub>6</sub>alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C<sub>1</sub>-C<sub>6</sub>alkoxy, hydroxy, cyano and benzyl, aryl, benzyl, heteroaryl, or aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group  
15 consisting of OH, halogen, CN, NO<sub>2</sub>, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio and C<sub>1</sub>-C<sub>12</sub>haloalkylthio;

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R<sub>9</sub> represents H, OH, SH, -N(R<sub>5</sub>)<sub>2</sub> (wherein the two R<sub>5</sub> are independently of each other), C<sub>1</sub>-C<sub>24</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>hydroxyalkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkoxy-C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkenyloxy, C<sub>2</sub>-C<sub>8</sub>alkynyloxy, -X-C<sub>1</sub>-C<sub>6</sub>alkyl-C(=O)R<sub>7</sub>,  
25 -C<sub>1</sub>-C<sub>6</sub>alkyl-S(=O)<sub>2</sub>R<sub>8</sub>, aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocycliloxy, or aryl, benzyl, heterocyclyl, aryloxy, benzyloxy or heterocycliloxy, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted in the ring independently of one another by  
30 halogen, NO<sub>2</sub>, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkyl or C<sub>1</sub>-C<sub>6</sub>haloalkoxy;

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X represents O, S, NH or N-C<sub>1</sub>-C<sub>6</sub>alkyl; and

Y represents O or S.

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Furthermore, preference is given to

(9) a compound according to any one of groups (1) to (8), wherein R<sub>1</sub> is isopropyl, or sec-butyl;

10 (10) a compound according to any one of groups (1) to (8), wherein R<sub>1</sub> is cyclohexyl;

(11) a compound according to any one of groups (1) to (8), wherein R<sub>1</sub> is 1-methyl-butyl;

15 (12) a compound according to any one of groups (1) to (11), wherein the bond between carbon atoms 22 and 23 is a single bond;

(13) a compound according to any one of groups (1) to (11), wherein the bond between carbon atoms 22 and 23 is a double bond;

20 (14) a compound according to any one of groups (1) to (13), wherein m is 1;

(15) a compound according to any one of groups (1) to (13), wherein m is 0;

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- (16) a compound according to any one of groups (1) to (15), wherein the configuration of the carbon atom at the  $\epsilon$ -position is (S);
- (17) a compound according to any one of groups (1) to (15), wherein the configuration of the carbon atom at the  $\epsilon$ -position is (R);
- (18) a compound according to any one of groups (1) to (6) and (8) to (17), wherein  $R_2$  is -CH<sub>3</sub>, -CH=CH<sub>2</sub>, -C $\equiv$ N, H<sub>2</sub>C=CH-CH<sub>2</sub>-, -C $\equiv$ CH or (CH<sub>3</sub>)<sub>2</sub>CHNHC(O);
- (19) a compound according to any one of groups (1) to (6) and (9) to (18), wherein  $R_3$  is H, -CH<sub>3</sub>, -C(O)CH<sub>3</sub>, -C(O)CH<sub>2</sub>CH<sub>3</sub>, -C(O)CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -C(O)CH<sub>2</sub>OCH<sub>3</sub>, -C(O)CH<sub>2</sub>OCH<sub>2</sub>CH<sub>3</sub>, -C(O)OCH<sub>3</sub> or -C(O)H;
- (20) a compound according to any one of groups (1) to (7) and (9) to (19), wherein  $R_4$  is either H or -CH<sub>3</sub>;
- (21) a compound according to any one of groups (1) to (3), (6), (7), (9) to (17), and (20), wherein  $R_2$  and  $R_3$  together either represent -CH<sub>2</sub>CH<sub>2</sub>CH=CHCH<sub>2</sub>- or -CH<sub>2</sub>CH=CHCH<sub>2</sub>-; or
- (22) a compound according to any one of groups (1) to (4) and (8) to (18), wherein  $R_3$  and  $R_4$  together either represent -CH<sub>2</sub>CH<sub>2</sub>CH=CHCH<sub>2</sub>- or -CH<sub>2</sub>CH=CHCH<sub>2</sub>-.

A preferred compound of formula (I) is where  $R_1$  is isopropyl or sec-butyl,  $m$  is 1, the stereochemistry at the  $\epsilon$ -position is (S),  $R_2$  is a group containing 1 to 3 carbon atoms,  $R_3$  is hydrogen or a group containing 1 to 4 carbon atoms and one or two oxygen atoms and  $R_4$  is hydrogen or a group containing 1 to 3 carbon atoms.

Where the same general group (or radical or substituent) type is described as present in a compound in two or more positions, the specific groups may be the same or different.

Further, where a number range of substitution is indicated, for example, mono- to

- 5 pentasubstituted C<sub>1</sub> to C<sub>12</sub>alkyl, a skilled person would understand that extent of substitutions would depend on the availability of substitution sites. Unless defined otherwise, the general terms used in the present application have the meanings given below:

- 10 Chemical constituent, preferably an organic group, is a group of atoms attached *via* an atom selected from carbon, nitrogen, sulfur, oxygen, or phosphorus. Preferably the attaching atom is carbon, nitrogen, sulfur or oxygen. Examples include unsubstituted and substituted hydrocarbyl groups, carbonate and derivatives, nitrate and derivatives, phosphate and derivatives, sulfate and derivatives, OH, amine and derivatives, alkoxy
- 15 groups, thio groups, sulfinyl groups and sulfonyl groups.

- Hydrocarbyl group is a group of atoms attached *via* a carbon atom. The group contains one or more carbon atoms and one or more hydrogen atoms, which group can be aliphatic, alicyclic, (each saturated or unsaturated), aromatic, straight-chained, branched-chained, or
- 20 a group with a combination thereof. Examples include methyl, ethyl, isopropyl, cyclohexyl, vinyl, ethynyl, allyl, phenyl, or benzyl. Preferably a hydrocarbyl group contains 1 to 15, more preferably 1 to 12, especially 1 to 4, such as 1 or 2, carbon atoms.

- Substituted hydrocarbyl group is a group of atoms attached *via* a carbon atom. The group
- 25 contains one or more carbon atoms, optionally one or more hydrogen atoms, and one or more hetero atoms, such as a halogen, boron, oxygen, nitrogen, sulfur, phosphorus, or a mixture thereof. Examples include cyano, halogen substituted carbon-containing groups, alkoxy groups, heterocyclic groups, such as pyridine and derivatives thereof, and carbonyl containing groups. Preferably a substituted hydrocarbyl group contains 1 to 15, more
- 30 preferably 1 to 12, especially 1 to 4, such as 1 to 2, carbon atoms.



Unless defined otherwise, carbon-containing groups (for example, alkyl, alkenyl, cycloalkyl) contain 1 up to and including 6; preferably 1 up to and including 4, in particular 1 or 2, carbon atoms.

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Halogen - as a group per se and also as a structural element of other groups and compounds, such as haloalkyl, haloalkoxy and haloalkylthio - is fluorine, chlorine, bromine or iodine, in particular fluorine, chlorine or bromine, especially fluorine or chlorine.

- 10 Alkyl - as a group per se and also as a structural element of other groups and compounds, such as haloalkyl, alkoxy and alkylthio - is, in each case taking into account the number of carbon atoms contained in each case in the group or compound in question, either straight-chain, *i.e.*, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl or octyl, or branched, for example, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl or isohexyl.
- 15 Preferred number of carbon atoms in an alkyl group is between 1 to 6, such as 1 to 4.

- Cycloalkyl - as a group per se and also as a structural element of other groups and compounds, such as, for example, of halocycloalkyl, cycloalkoxy and cycloalkylthio - is, in each case taking into account the number of carbon atoms contained in each case in the group or compound in question, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl. Preferred number of carbon atoms in a cycloalkyl group is between 3 to 6, such as 3 to 4.
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- Alkenyl - as a group per se and also as a structural element of other groups and compounds - is, taking into account the number of carbon atoms and conjugated or isolated double bonds contained in the group, either straight-chain, for example, vinyl, allyl, 2-butenyl, 3-pentenyl, 1-hexenyl, 1-heptenyl, 1,3-hexadienyl or 1,3-octadienyl, or branched, for example, isopropenyl, isobutenyl, isoprenyl, tert-pentenyl, isohexenyl, isoheptenyl or
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isooctenyl. Preference is given to alkenyl groups having 3 to 12, in particular 3 to 6, especially 3 or 4, carbon atoms.

Alkynyl – as a group per se and also as a structural element of other groups and  
5 compounds - is, in each case taking into account the number of carbon atoms and  
conjugated or isolated double bonds contained in the group or compound in question, either  
straight-chain, for example, ethynyl, propargyl, 2-butyne, 3-pentyne, 1-hexyne, 1-heptyne,  
3-hexen-1-ynyl or 1,5-heptadien-3-ynyl, or branched, for example, 3-methylbut-1-ynyl,  
4-ethylpent-1-ynyl, 4-methylhex-2-ynyl or 2-methylhept-3-ynyl. Preference is given to  
10 alkynyl groups having 3 to 12, in particular 3 to 6, especially 3 or 4, carbon atoms.

Alkoxy - as a group per se and also as a structural element of other groups and compounds  
is, in each case taking into account the number of carbon atoms contained in each case in  
the group or compound in question, either straight-chain, e.g., methoxy, ethoxy or propoxy,  
15 or branched-chain, for example, isopropoxy, isobutoxy, or sec-butoxy. One or more  
oxygen atoms can be present in the group. Preferred number of carbon atoms in an alkoxy  
group is between 1 to 6, such as 1 to 4. Similarly, the oxygen atom in the group alkenyloxy  
or alkynyloxy can be in any position and the preferred number of carbon atoms in either  
group is between 2 to 6, such as 2 to 4.

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Halogen-substituted carbon-containing groups and compounds, such as, for example,  
halogen-substituted alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or alkylthio, can be partially  
halogenated or perhalogenated, where in the case of polyhalogenation the halogen  
substituents can be identical or different. Examples of haloalkyl - as a group per se and  
25 also as a structural element of other groups and compounds, such as haloalkoxy or  
haloalkylthio - are methyl which is mono- to trisubstituted by fluorine, chlorine and/or  
bromine, such as  $\text{CHF}_2$  or  $\text{CF}_3$ ; ethyl which is mono- to pentasubstituted by fluorine,  
chlorine and/or bromine, such as  $\text{CH}_2\text{CF}_3$ ,  $\text{CF}_2\text{CF}_3$ ,  $\text{CF}_2\text{CCl}_3$ ,  $\text{CF}_2\text{CHCl}_2$ ,  $\text{CF}_2\text{CHF}_2$ ,  
 $\text{CF}_2\text{CFCl}_2$ ,  $\text{CF}_2\text{CHBr}_2$ ,  $\text{CF}_2\text{CHClF}$ ,  $\text{CF}_2\text{CHBrF}$  or  $\text{CClFCHClF}$ ; propyl or isopropyl which is  
30 mono- to heptasubstituted by fluorine, chlorine and/or bromine, such as  $\text{CH}_2\text{CHBrCH}_2\text{Br}$ ,  
 $\text{CF}_2\text{CHFCH}_2\text{F}$ ,  $\text{CH}_2\text{CF}_2\text{CF}_3$ ,  $\text{CF}(\text{CF}_3)_2$  or  $\text{CH}(\text{CF}_3)_2$ ; butyl or one of its isomers, mono- to

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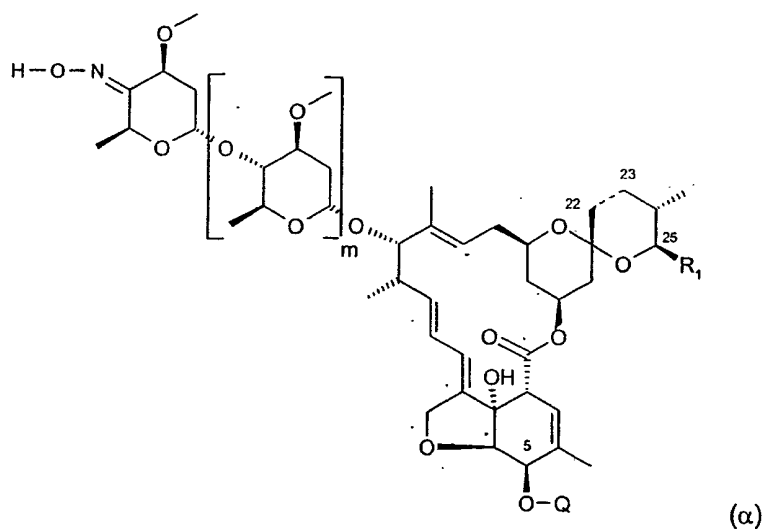
- nonasubstituted by fluorine, chlorine and/or bromine, such as  $\text{CF}(\text{CF}_3)\text{CHF}\text{CF}_3$  or  $\text{CH}_2(\text{CF}_2)_2\text{CF}_3$ ; pentyl or one of its isomers, mono- to undecasubstituted by fluorine, chlorine and/or bromine, such as  $\text{CF}(\text{CF}_3)(\text{CHF}_2)\text{CF}_3$  or  $\text{CH}_2(\text{CF}_2)_3\text{CF}_3$ ; and hexyl or one of its isomers, mono- to tridecasubstituted by fluorine, chlorine and/or bromine, such as
- 5  $(\text{CH}_2)_4\text{CHBrCH}_2\text{Br}$ ,  $\text{CF}_2(\text{CHF})_4\text{CF}_3$ ,  $\text{CH}_2(\text{CF}_2)_4\text{CF}_3$  or  $\text{C}(\text{CF}_3)_2(\text{CHF})_2\text{CF}_3$ .

Aryl is in particular phenyl, naphthyl, anthracenyl, phenanthrenyl, perylenyl or fluorenyl, preferably phenyl.

- 10 Heterocyclyl is understood as being a three- to seven-membered monocyclic ring, which may be saturated or unsaturated, and that contains from one to three hetero atoms selected from the group consisting of B, N, O and S, especially N and S; or a bicyclic ring system having from 8 to 14 ring atoms, which may be saturated or unsaturated, and that may contain either in only one ring or in both rings independently of one another, one or
- 15 two hetero atoms selected from N, O and S; heterocyclyl is in particular piperidinyl, piperazinyl, oxiranyl, morpholinyl, thiomorpholinyl, pyridyl, N-oxidopyridinio, pyrimidyl, pyrazinyl, s-triazinyl, 1,2,4-triazinyl, thienyl, furanyl, dihydrofuranyl, tetrahydrofuranyl, pyranal, tetrahydropyranal, pyrrolyl, pyrrolinyl, pyrrolidinyl, pyrazolyl, imidazolyl, imidazolinyl, thiazolyl, isothiazolyl, triazolyl, oxazolyl, thiadiazolyl, thiazolinyl, thiazolidinyl, oxadiazolyl,
- 20 dioxaborolanyl, phthalimidoyl, benzothienyl, quinolinyl, quinoxalinyl, benzofuranyl, benzimidazolyl, benzpyrrolyl, benzthiazolyl, indolinyl, isoindolinyl, cumarinyl, indazolyl, benzothiophenyl, benzofuranyl, pteridinyl or purinyl, which are preferably attached via a C atom; thienyl, benzofuranyl, benzothiazolyl, tetrahydropyranal, dioxaborolanyl, or indolyl is preferred; in particular dioxaborolanyl, pyridyl or thiazolyl. The said heterocyclyl radicals
- 25 may preferably be unsubstituted or – depending on the substitution possibilities on the ring system - substituted by 1 to 3 substituents selected from the group consisting of halogen, =O, -OH, =S, SH, nitro,  $\text{C}_1\text{-C}_6\text{alkyl}$ ,  $\text{C}_1\text{-C}_6\text{hydroxyalkyl}$ ,  $\text{C}_1\text{-C}_6\text{alkoxy}$ ,  $\text{C}_1\text{-C}_6\text{haloalkyl}$ ,  $\text{C}_1\text{-C}_6\text{haloalkoxy}$ , phenyl and benzyl.
- 30 The invention also provides a process for preparing a compound of the formula (I) via a sulfinimine, nitron or cyanide or by an Ugi reaction.

*Sulfinimine*

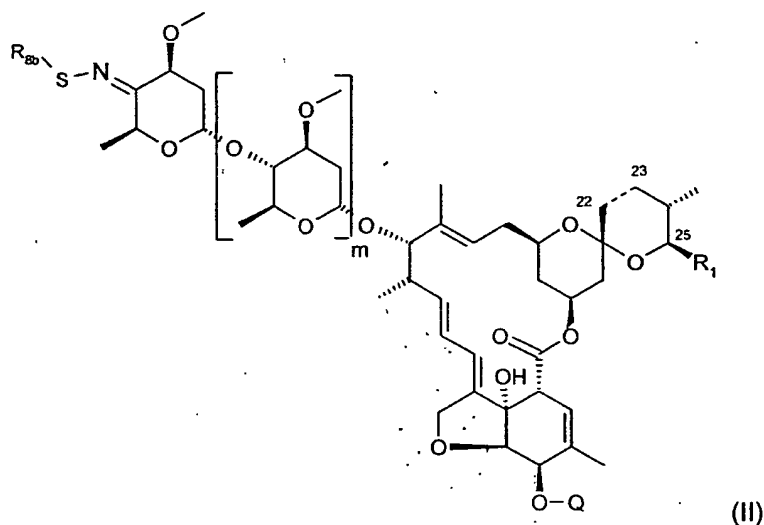
(A) Advantageously, 4'' or 4' oxime avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula ( $\alpha$ ) below) is used as a starting material.



wherein R<sub>1</sub>, m and the bond between carbon atoms 22 and 23 is as defined for a compound of formula (I) of the first aspect, Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position, and the double bond between the carbon atom at the 4' or 4'' position and nitrogen atom is E or Z configuration.

The oxime is reacted with a suitable disulfide and an aliphatic or aromatic phosphine to form the corresponding sulfenimine derivative of formula (II)

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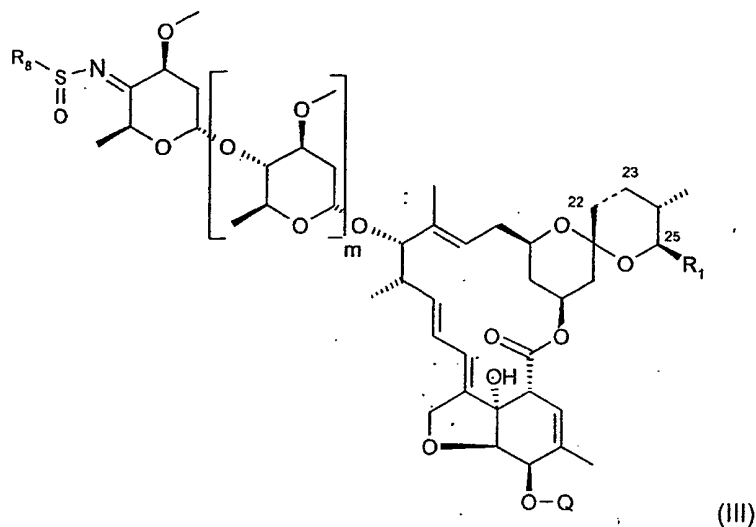
(II)

wherein  $R_1$ ,  $m$ , and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect,  $R_{bb}$  is as defined for  $R_8$  in compound of formula (I) of the first aspect,  $Q$  is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position, and the double bond between the carbon atom at the 4' or 4'' position and nitrogen atom is E or Z configuration. Derek H. Barton, William B. Motherwell, Ethan S. Simon, Samir Z. Zard *J. Chem. Soc. Trans. I* **1986**, 2243-2252 provides background on the general reaction;

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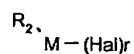
(B) the compound of formula (II) is oxidised with a suitable oxidant to form sulfinimine derivative of formula (III)

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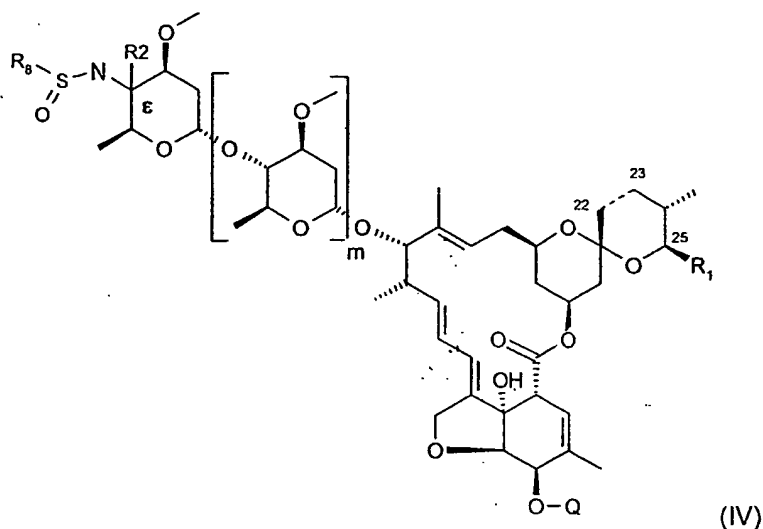
wherein  $R_1$ ,  $m$ ,  $R_8$  and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect,  $Q$  is a suitable protecting group to prevent reaction on the oxygen atom on 5-carbon position, and the double bond between the carbon atom at the 4' or 4'' position and nitrogen atom is E or Z configuration;

(C) the compound or derivative of formula (III) is reacted with an organometallic reagent, for example, of formula



10 wherein  $R_2$  is as defined for compound of formula (I) of the first aspect and  $M$  is a metal atom, preferably magnesium, lithium or cerium, and  $Hal$  is a halogen atom, preferably chlorine, bromine or iodine and  $r$  is 0 to 2 as function of the metal charge (such a reagent is known or can be prepared by methods known) to yield a sulfinamide compound of formula (IV)

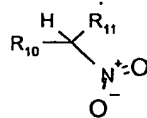
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wherein  $R_1$ ,  $m$ ,  $R_2$ ,  $R_8$  and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, and  $Q$  is a suitable protecting group to prevent reaction on the oxygen atom on 5-carbon position; or

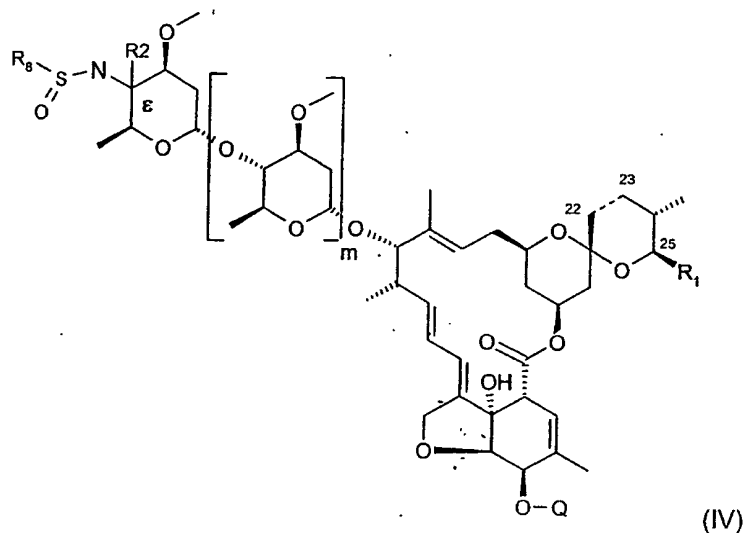
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(D) the compound or derivative of formula (III) is reacted with a nitro alkyl reagent, for example, of formula



- where  $R_{10}$  and  $R_{11}$  are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted  $C_1-C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3-C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2-C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2-C_{12}$ alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted  $C_3-C_{12}$ cycloalkyl ester, an unsubstituted or mono- to pentasubstituted  $C_1-C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1-C_{12}$ alkyl sulfone or unsubstituted or mono- to pentasubstituted  $C_1-C_{12}$ alkyl nitrile, to yield a sulfinamide compound of formula (IV)

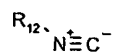
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wherein  $R_1$ ,  $m$ ,  $R_2$ ,  $R_8$  and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, and  $Q$  is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or

5

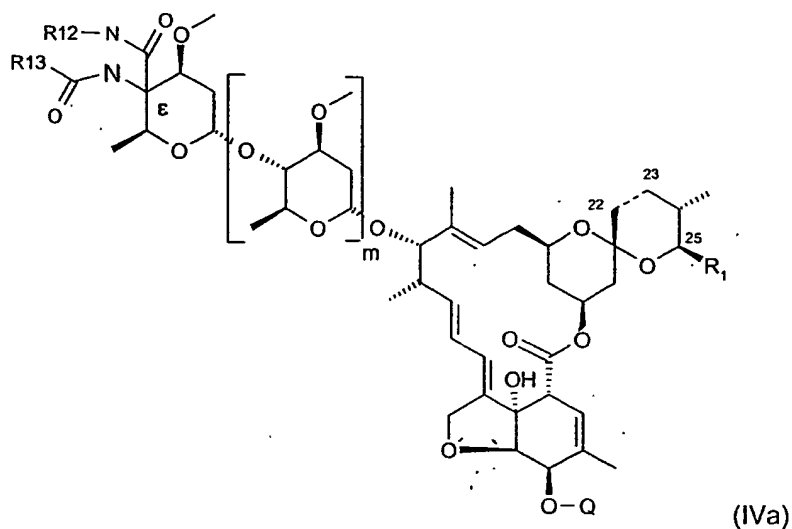
(E) the compound or derivative of formula (III) is reacted with an isocyanate reagent, for example, of formula



where  $R_{12}$  is unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl ester, an unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl sulfone or unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl nitrile, to yield an amide compound of formula (IVa).



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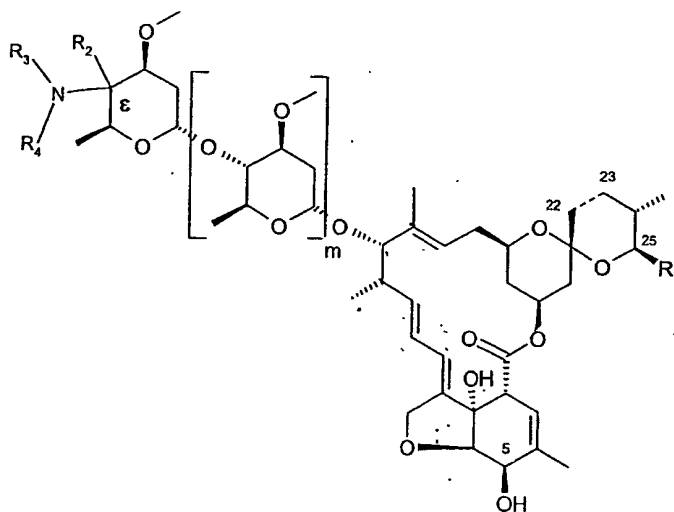


wherein R<sub>1</sub>, m and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, R<sub>12</sub> is as defined above, and R<sub>13</sub> is unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl coming from the carboxylic acid used as reagent, and Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; and

either

(F) the sulfinyl group and the protecting group Q are removed either in one step or one after another depending on the strength of the deprotecting agent, for example, an acidic and/or fluorine reagent, to yield a compound of formula (I)

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wherein  $R_1$ ,  $R_2$ ,  $m$ , and the bond between carbon atoms 22 and 23 are as defined above in the first aspect, and  $R_3$  and  $R_4$  each represent hydrogen;

5 or

(G) the sulfinyl group is only removed and reactions are carried out to modify the groups  $R_2$ ,  $R_3$  and  $R_4$ , for example, by reacting a reagent of the formula  $R\text{-Hal}$  (where  $R$  is as chemical constituent, preferably  $R$  is unsubstituted or mono- to pentasubstituted  $C_1\text{-}C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3\text{-}C_{12}$ cycloalkyl, unsubstituted or  
 10 mono- to pentasubstituted  $C_2\text{-}C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2\text{-}C_{12}$ alkynyl, in each of these cases, one or more  $\text{CH}_2$  groups may be replaced by  $\text{C(O)}$ ,  $\text{C(S)}$ ,  $\text{C(O)O}$ ,  $\text{C(S)O}$  and  $\text{Hal}$  is halogen, especially chlorine, bromine or iodine), and thereafter removing the protecting group at oxygen atom at the 5-carbon position to yield a compound of formula (I).

15

or

(H) if the sulfinyl group is removed during the Step before (for example during Step E), the  $R_{13}\text{C(O)}$  is removed by reaction with a reducing reagent and reactions are carried out to modify the groups  $R_2$ ,  $R_3$  and  $R_4$ , for example, by reaction with a reagent of the formula  $R\text{-Hal}$  (where  $R$  is as chemical constituent, preferably unsubstituted or mono- to  
 20

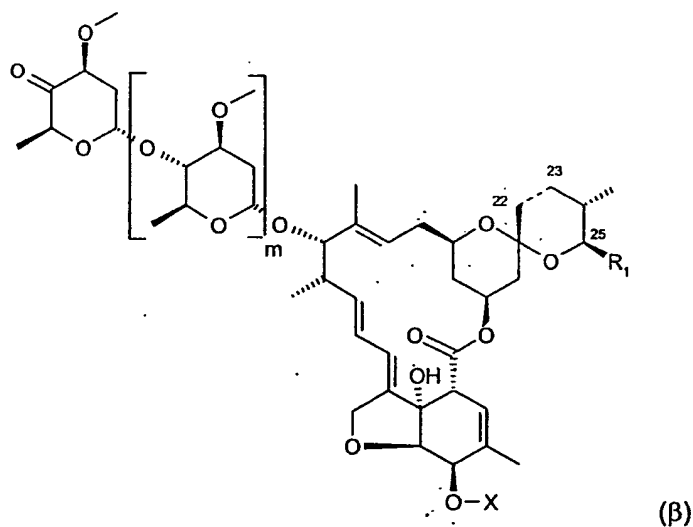
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pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl, unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkenyl or unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkynyl where, in each of these cases, one or more CH<sub>2</sub> groups may be replaced by C(O); C(S), C(O)O or C(S)O, and Hal is halogen, especially chlorine, 5 bromine or iodine), and thereafter removing the protecting group on the oxygen atom at the 5-carbon position to yield a compound of formula (I).

In an embodiment, R<sub>8b</sub> is C<sub>1</sub>-C<sub>6</sub>alkyl that is optionally substituted with one to five substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub>alkoxy, hydroxy, and aryl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, aryl, or aryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, C<sub>1</sub>-C<sub>12</sub>alkyl, and C<sub>1</sub>-C<sub>12</sub>alkoxy;

### Nitrone

(l) Preferably, 4'' or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula ( $\beta$ ) below) is used as a starting material.

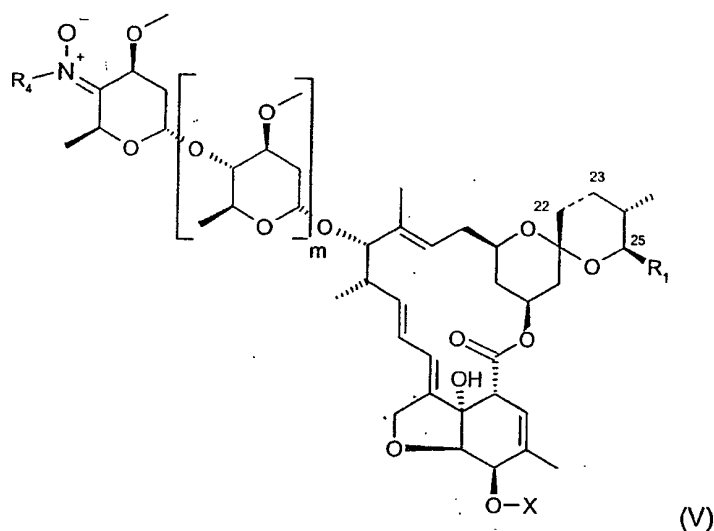


wherein R<sub>1</sub>, m and the bond between carbon atoms 22 and 23 is as defined for a compound of formula (I) of the first aspect, and X represents H or Q (a suitable protecting group to prevent reaction of the oxygen atom at the 5-carbon position). The preparation of

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such a starting material is described in EP-A-0343708, and briefly involves oxidation of the 4'' or 4' hydroxyl group of avermectin or avermectin monosaccharide respectively. It is preferred that X represents Q.

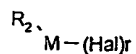
- 5 The oxo derivative is reacted with a N-R<sub>4</sub>hydroxylamine, preferably a N-hydrocarbylhydroxylamine hydrochloride, to yield a nitron compound of formula (V)



- wherein R<sub>1</sub>, R<sub>4</sub>, m, and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, X is as defined for formula (β), and the double bond between the carbon atom at the 4' or 4'' position and nitrogen atom is E or Z;
- 10

either

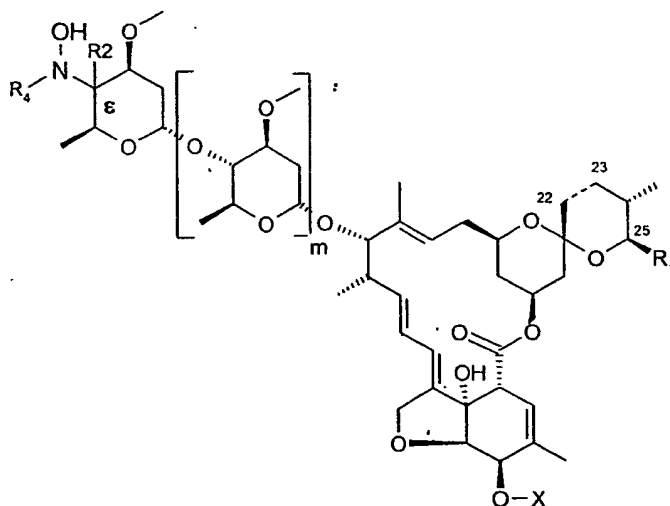
- (J) the compound of formula (V) is reacted with an organometallic or a silyl reagent, for example, of formula
- 15



wherein R<sub>2</sub> is as defined for compound of formula (I) and M is a metal atom, preferably magnesium, lithium, cerium or silicon and Hal is a halogen atom, preferably chlorine,

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bromine or iodine and  $r$  is 0 to 2 as function of the metal charge (such a reagent is known or can be prepared by methods known) or  $r$  is 0 in the case of silicon to yield a N- $R_4$ hydroxyamino compound of formula (VI)



(VI)

wherein  $R_1$ ,  $R_2$ ,  $R_4$ ,  $m$  and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) and  $X$  is as defined for formula (β), and the ( $R$ ) isomer at  $\epsilon$  position is preferably obtained; and

10 either

(K) remove the protecting group  $Q$ , if present, to yield a compound of formula (I), wherein  $R_1$ ,  $R_2$ ,  $R_4$ ,  $m$  and the bond between carbon atoms 22 and 23 are as defined in the first aspect, and  $R_3$  is OH; or

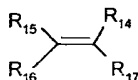
15 (L) carry out reactions on one or more of  $R_2$ ,  $R_3$  and  $R_4$  groups to modify the group, for example, by reacting the compound of formula (VI) with a reagent of formula  $Hal-R$ , where  $R$  is a chemical constituent, preferably  $R$  is unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted

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C<sub>2</sub>-C<sub>12</sub>alkynyl, in each of these cases, one or more CH<sub>2</sub> groups may be replaced by C(O), C(S), C(O)O, C(S)O and Hal is halogen, especially chlorine, bromine or iodine; and remove the protecting group Q, if present, to yield a compound of formula (I) wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, m and the bond between carbon atoms 22 and 23 are as defined in the first aspect, and  
 5 then and removing the protecting group Q, if present, to yield a compound of formula (I);

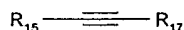
or

(M) the compound of formula (V) is reacted with a reagent of formula



10

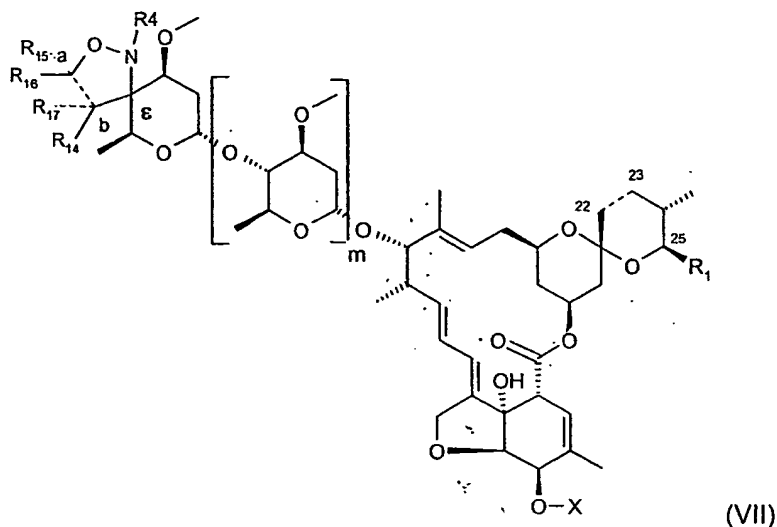
or



15

where R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl, unsubstituted or mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkenyl, unsubstituted or  
 15 mono- to pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkynyl, unsubstituted or mono- to pentasubstituted aromatic, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl sulfone, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl nitrile, to yield a N-isoxazolidine or 2,3-dihydro-isoxazole compound of formula (VII)

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- wherein R<sub>1</sub>, R<sub>4</sub>, m and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I), and the bond between carbon atoms a and b is a double or a single bond (depending on whether an alkene or an alkyne reagent is used) and R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are as defined above and X is as defined for formula (β); the (*R*) isomer at ε position is preferably obtained, and the carbon a or b could (*R*) or (*S*); and

- (N) remove the protecting group Q, if present, to yield a compound of formula (I), wherein R<sub>1</sub>, R<sub>4</sub>, m and the bond between carbon atoms 22 and 23 are as defined in the first aspect and R<sub>2</sub> and R<sub>3</sub> is an alkylene or alkenylene bridge with an oxygen atom attached to the nitrogen atom attached to the 4' or 4'' position.

### Cyanide

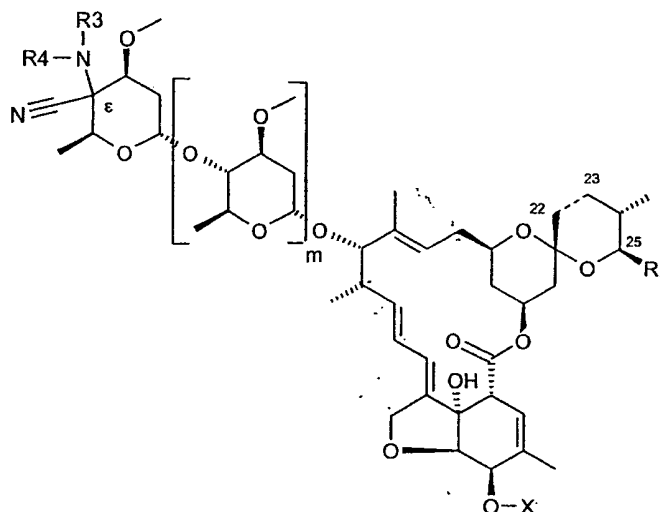
- (O) Preferably, 4'' or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (β) see F) is used as a starting material.

The compound of formula (β) is reacted with a silylated amine, such as hexamethyldisilylazane or heptamethyldisilylazane, in presence of a Lewis acid and a trialkylsilyl cyanide, such as trimethylsilyl cyanide, to yield a compound of formula (VIII).

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Alternatively, the compound of formula ( $\beta$ ) is reacted with an amine of formula  $R_3R_4NH$ , a chlorosilane, a Lewis acid and a trialkylsilyl cyanide; such as trimethylsilyl cyanide, to yield a compound of formula (VIII).

5



(VIII)

wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $m$ , and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I),  $X$  is as defined for formula ( $\beta$ ), and the protecting group  $Q$ , if present, is removed to yield a compound of formula (I) wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $m$  and the bond between carbon atoms 22 and 23 are as defined in formula (I) and is  $R_2$  is CN; or

(P) carry out reactions on one or both of  $R_3$  and  $R_4$  groups to modify the group by reacting the compound of formula (VIII) with a reagent, such as of formula Hal-R, where  $R$  is a chemical constituent, preferably  $R$  is unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, in each of these cases, one or more  $CH_2$  groups may be replaced by  $C(O)$ ,  $C(S)$ ,  $C(O)O$ ,  $C(S)O$  and Hal is halogen, especially chlorine, bromine or iodine; and remove the protecting group  $Q$ , if present, to yield a compound of formula (I) wherein  $R_1$ ,  $R_3$ ,  $R_4$ ,  $m$

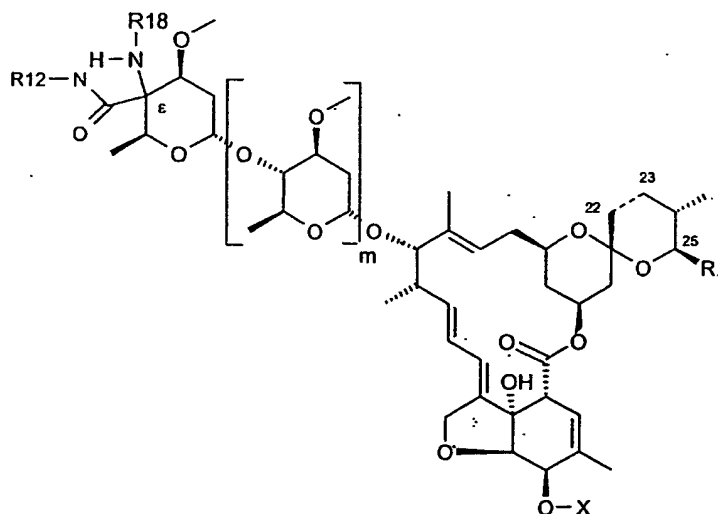


and the bond between carbon atoms 22 and 23 are as defined in formula (I) and is R<sub>2</sub> is CN.

### Ugi Reaction

- 5 (Q) Preferably, 4'' or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (β) see I) is used as a starting material.

The compound of formula (β) is reacted with an ammonium salt of formula  $R_{18}CO_2NH_4^+$  (where  $R_{18}$  is H, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl ester, an unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl sulfone or unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl nitrile), an isocyanide of formula  $R_{12}NC$  (see E) to yield a compound of formula (IX).



(IX)

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wherein  $R_1$ ,  $m$ , and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I),  $X$  is as defined for formula ( $\beta$ ), and the protecting group  $Q$ , if present, is removed to yield a compound of formula (I) wherein  $R_1$ ,  $R_3$ ,  $m$  and the bond between carbon atoms 22 and 23 are as defined in formula (I),  $R_2$  is  $R_{12}NHC(O)$  and  $R_4$  is

5  $R_{18}C(O)$ .

Compounds of formula (I) can themselves be used as starting materials for further reactions so that further derivatives can be prepared, for example, by altering the groups  $R_2$ ,  $R_3$  and  $R_4$  by suitable known reactions, such as alkylation, acylation, metathesis, palladium coupling reactions, addition of organometallics.

10

The preparation of avermectin monosaccharide derivatives of formula (I) follow the process steps described above, but from the corresponding monosaccharide derivative.

15 The comments made above in connection with tautomer or diastereoisomer of compound of formula (I) applies analogously to the starting materials mentioned in respect of their tautomers and diastereoisomers.

The conditions for reactions described are carried out in a manner known *per se*, for example in the absence or, customarily, in the presence of a suitable solvent or diluent or of a mixture thereof, the reactions being carried out, as required, with cooling, at room temperature or with heating, for example, in a temperature range of approximately from -80°C to the boiling temperature of the reaction medium, preferably from approximately 0°C to approximately +150°C, and, if necessary, in a closed vessel, under pressure, under an inert gas atmosphere and/or under anhydrous conditions. Especially advantageous reaction conditions can be found in the Example section.

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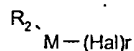
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The reaction time is not critical; a reaction time of from about 0.1 to about 24 hours, especially from about 0.5 to about 10 hours, is preferred.

The product is isolated by customary methods, for example by means of filtration,  
 5 crystallization, distillation or chromatography, or any suitable combination of such methods.

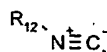
The organometallic reagent used in steps (C) and (J) of formula



is known or can be prepared by methods known. A suitable example is a Grignard reagent.

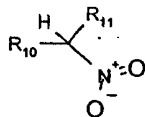
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The isocyanate reagent used in step (E) and step (Q) of formula



is known or can be prepared by methods known.

The nitroalkyl reagent used in step (D) of formula



15

is known or can be prepared by methods known.

It is generally useful to protect oxygen at the 5-carbon position to prevent reaction on that position when carrying out reactions with avermectin and avermectin monosaccharide.

20 Protecting groups include: alkyl ether radicals, such as methoxymethyl, methylthiomethyl, tert-butylthiomethyl, benzyloxymethyl, p-methoxybenzyl, 2-methoxyethoxymethyl, 2,2,2-trichloroethoxymethyl, 2-(trimethylsilyl)ethoxymethyl, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 1-methyl-1-methoxyethyl, 1-

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methyl-1-benzyloxyethyl, trichloroethyl, 2-trimethylsilylethyl, tert-butyl, allyl, p-methoxyphenyl, 2,4-dinitrophenyl, benzyl, p-methoxybenzyl, o-nitrobenzyl, p-nitrobenzyl, triphenylmethyl; trialkylsilyl radicals, such as trimethylsilyl, triethylsilyl, dimethyl-tert-butylsilyl, dimethyl-isopropylsilyl, dimethyl-1,1,2-trimethylpropylsilyl, diethyl-isopropylsilyl, 5 dimethyl-tert-hexylsilyl, but also phenyl-tert-alkylsilyl groups, such as diphenyl-tert-butylsilyl; esters, such as formates, acetates, chloroacetates, dichloroacetates, trichloroacetates, trifluoroacetates, methoxyacetates, phenoxyacetates, pivaloates, benzoates; alkyl carbonates, such as methyl-, 9-fluorenylmethyl-, ethyl-, 2,2,2-trichloroethyl-, 2-(trimethylsilyl)ethyl-, vinyl-, allyl-, benzyl-, p-methoxybenzyl-, o-nitrobenzyl-, p-nitrobenzyl-, 10 but also p-nitrophenyl-carbonate.

Preference is given to trialkylsilyl radicals, such as trimethylsilyl, triethylsilyl, dimethyl-tert-butylsilyl, diphenyl-tert-butylsilyl, esters, such as methoxyacetates and phenoxyacetates, and carbonates, such as 9-fluorenylmethylcarbonates and allylcarbonates. Dimethyl-tert- 15 butylsilyl ether is especially preferred.

Once the desired reactions are completed, the reagents used for removing the protecting group depends on the strength of the protecting group used. There are suitable for the removal of the protecting group Lewis acids, such as hydrochloric acid, methanesulfonic 20 acid,  $\text{BF}_3 \cdot \text{OEt}_2$ , HF in pyridine,  $\text{Zn}(\text{BF}_4)_2 \cdot \text{H}_2\text{O}$ , p-toluenesulfonic acid,  $\text{AlCl}_3$ ,  $\text{HgCl}_2$ ; ammonium fluoride, such as tetrabutylammonium fluoride; bases, such as ammonia, trialkylamine or heterocyclic bases; hydrogenolysis with a catalyst, such as palladium-on-carbon; reducing agents, such as sodium borohydride or tributyltin hydride with a catalyst, such as  $\text{Pd}(\text{PPh}_3)_4$ , or also zinc with acetic acid. Preference is given to acids, such as 25 methanesulfonic acid or HF in pyridine; sodium borohydride with Pd(0); bases, such as ammonia, triethylamine or pyridine; especially acids, such as HF in pyridine or methanesulfonic acid. Generally, an acidic reagent, such as a mixture of methanesulfonic acid in methanol or a HF in pyridine, is effective in removing dimethyl-tert-butylsilyl ether group from oxygen at the 5-carbon position. A less acidic reagent, such as a mixture of 30 alcohol (e.g., isopropanol) and trifluoroacetic acid in a solvent (e.g., THF), is not adequate, but it is generally sufficient to remove the sulfinyl group in step (F)

The starting materials mentioned that are used for the preparation of the compound of formula (I), the intermediates therefor (e.g., the compound of formula (II), (III) or (V)), and, where applicable, their tautomers are known or can be prepared by methods known *per se*.

5

The process steps (A) to (Q) described above are detailed further below:

Process step (A):

Examples of solvents and diluents include: aromatic, aliphatic and alicyclic hydrocarbons and halogenated hydrocarbons, such as benzene, toluene, xylene, mesitylene, tetralin, chlorobenzene, dichlorobenzene, bromobenzene, petroleum ether, hexane, cyclohexane, 10 dichloromethane, trichloromethane, tetrachloromethane, dichloroethane, trichloroethene or tetrachloroethene; ethers, such as diethyl ether, dipropyl ether, diisopropyl ether, dibutyl ether, tert-butyl methyl ether, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, ethylene glycol dimethyl ether, dimethoxydiethyl ether, tetrahydrofuran or dioxane; 15 esters of carboxylic acids, such as ethyl acetate; amides, such as dimethylformamide, dimethylacetamide or 1-methyl-2-pyrrolidinones; nitriles, such as acetonitrile; nitroalkyls, such as nitromethane; sulfoxides, such as dimethyl sulfoxide; or mixtures of the mentioned solvents. Preference is given to ether, such as tetrahydrofuran and diethyl ether, especially tetrahydrofuran.

20

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 25°C.

A preferred disulfide is a carbon-containing disulfide, for example, dialiphatic disulfide, dialicyclic disulfide, diaromatic disulfide, such as di-tert-butyl disulfide, di-tert-amyl disulfide, di-tert-dodecyl disulfide, diphenyl disulfide, p-tolyl disulfide, especially preferred is diphenyl disulfide. 25

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A preferred phosphine is trialkylphosphine, triarylphosphine, such as tributylphosphine, triethylphosphine, triphenylphosphine, especially preferred is tributylphosphine.

Especially preferred conditions for the reaction are described in Example P1 (step A).

5

Process step (B):

Examples of solvents and diluents are the same as those mentioned under Process step A. In particular, halogenated hydrocarbons, such as chloroform and dichloromethane and water are especially suitable.

10

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 25°C.

15

Examples of oxidant suitable for oxidizing the sulfinimine to a sulfinimine are hydrogen peroxide, arylperoxy acid, alkyl hydroperoxide, dimethyldioxirane, potassium peroxymonosulfate sulfate, sodium periodate, dialkylperoxide, 2-iodylbenzoic acid,  $\alpha$ -Cumene hydroperoxide, oxaziridine analogues; preferred is metachloroperbenzoic acid. The reaction is preferably carried out in biphasic system.

20

Especially preferred conditions for the reaction are described in Example P1 (step B).

Process step (C):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to ether, such as tetrahydrofuran and diethyl ether, especially tetrahydrofuran.

25

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The reactions are advantageously carried out in a temperature range of from approximately -100°C to 50°C, preferably at from -78°C to 25°C.

5 Especially preferred conditions for the reaction are described in Examples P1 (step C) or P2 (step A).

Process step (D):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to the use of the nitroalkyl reagent as solvent.

10 Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, dialkylamines, such as piperidine, and heterocyclic bases, such as pyridine.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 70°C, preferably at from -25°C to 50°C.

15

Especially preferred conditions for the reaction are described in Examples P21 (step A) or P23 (step A).

The process step for the removing of the protecting group Q is identical to the Process step (F).

20 Process step (E):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to polychloroalkane, such as dichloromethane.

25 Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, dialkylamines, such as piperidine, and heterocyclic bases, such as pyridine.



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Suitable acids are especially polyhalogenated carboxylic acid, such as trifluoroacetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid.

- The reactions are advantageously carried out in a temperature range of from approximately  
5 -80°C to 70°C, preferably at from -80°C to 50°C.

The process step for the removing of the protecting group Q is identical to the Process step (F).

- 10 Especially preferred conditions for the reaction are described in Examples P22 (step A).

Process step (F):

Examples of solvents and diluents are the same as those mentioned under Process step A.

- 15 In addition, alcohols, such as methanol, ethanol or 2-propanol, and water are suitable.

Suitable acids are especially polyhalogenated carboxylic acid, such as trifluoroacetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid; or alkylsulfonic acid, such as methanesulfonic acid; or source of anionic fluoride, such as hydrofluoric acid,

- 20 tetrabutylammonium fluoride, potassium fluoride, cesium fluoride.

The reactions are advantageously carried out in a temperature range of from approximately -100°C to 50°C, preferably at from -78°C to 25°C.

- 25 Especially preferred conditions for the reaction are described in Examples P1 (step D), P1 (step E), and P2 (step B).

Process step (G):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine or dimethylaminopyridine.

Especially preferred conditions for the reaction are described in Examples P5 (step A), P8 (step A), P9 (step A), P11 (step A), P12 (step A).

And the process step for the removing of the protecting group Q is identical to the Process step (F).

Process step (H):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ethers, such as tetrahydrofuran, halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate, and to mixtures of halogenated hydrocarbons and water and mixtures of esters of carboxylic acids and water.

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The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

5     Suitable reducing reagents are borane derivatives such as sodium borohydride and sodium cyanoborohydrate.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine or dimethylaminopyridine.

10

The process step for the removing of the protecting group Q is identical to the Process step (F).

Especially preferred conditions for the reaction are described in Examples P30 (step A, B).

15     Process step (I):

Examples of solvents and diluents are the same as those mentioned under Process step A. In addition, alcohols, such as methanol, ethanol or 2-propanol, are suitable. Preference is given to alcohols, such as methanol.

20     Examples of R<sub>4</sub>hydroxyamines are N-alkylhydroxylamines, N- cycloalkylhydroxylamines, N-arylhydroxylamines, N-benzylhydroxylamines, N-heteroarylhydroxylamines; specific examples include N-methylhydroxylamine.

25     Suitable bases are especially trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

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The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 40°C.

Especially preferred conditions for the reaction are described in Examples P3 (step A).

5

Process step (J):

Conditions described in Process step (C) are also applicable.

Especially preferred conditions for the reaction step are described in Example P3 (step B).

10

Process step (K):

Conditions described in Process step (F) are also applicable.

Especially preferred conditions for the reaction are described in Examples P3 (step C).

15

Process step (L):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

20

Suitable examples of R-Hal include alkyl halides, such as methyl iodide, and acyl halides such as acetyl chloride, and sulfonyl halide, such as sulfamoyl chloride or benzenesulfonyl

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chloride or methylsulfonyl chloride, and arylchloroformate, alkyl haloformate, such as methylchloroformate.

5 The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

10

Especially preferred conditions for the reaction are described in Example P7.

Process step (M):

15 Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to aromatic, such as toluene.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 150°C, preferably at from 0°C to 100°C.

20 Especially preferred conditions for the reaction are described in Examples P6 (step A).

Process step (N):

Conditions described in Process step (F) are also applicable.

25 Especially preferred conditions for the reaction are described in Examples P6 (step B).

Process step (O):

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Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to ester, such as ethyl acetate and to aromatic, such as toluene.

5 Suitable Lewis acids, for example, are aluminium chloride, tin tetrachloride, ferric chloride, boron trichloride, titanium chloride especially zinc derivatives, such as zinc chloride.

In alternative process, the amine is silylated *in situ* by addition of trialkylsilyl chloride, such as trimethylsilyl chloride.

10 The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 100°C.

Especially preferred conditions for the reaction are described in Examples P15 (step A), P16 (step A), P17 (step A), P18 (step A).

15

Process step (P):

20 Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

25

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

Especially preferred conditions for the reaction are described in Example P19 and P20.

Process step (Q):

- 5 Examples of solvents and diluents are the same as those mentioned under Process step A. In addition, alcohols, such as methanol, ethanol or 2-propanol, are suitable. Preference is given to alcohols, such as methanol.

- Suitable ammonium salts are especially ammonium salts derived from formic acid, alkyl carboxylic acid, such as acetic acid and polyhalogenated carboxylic acid, such as  
10 trifluoroacetic acid, chloroacetic acid, dichloroacetic acid and trichloroacetic acid.

The reactions are advantageously carried out in a temperature range of from approximately -80°C to 70°C, preferably at from -20°C to 50°C.

- 15 The compound of the invention may be in the form of one of possible isomers. Therefore, a preparation can result in mixture of isomers, *i.e.*, a diastereomeric mixture; the invention relates both to a pure isomer and to a diastereomeric mixture and is to be interpreted accordingly, even if stereochemical details are not mentioned specifically in every case.

- 20 A diastereomeric mixture can be resolved into the pure isomers by known methods, for example by recrystallisation from a solvent, by chromatography, for example, high pressure liquid chromatography (HPLC) on acetylcellulose, with the aid of suitable microorganisms, by cleavage with specific, immobilised enzymes, or *via* the formation of inclusion compounds, for example using crown ethers, only one isomer being complexed.

25

Apart from by separation of corresponding mixtures of isomers, pure diastereoisomers can be obtained according to the invention also by generally known methods of stereoselective

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synthesis, for example by carrying out the process according to the invention using starting materials having correspondingly suitable stereochemistry.

5 In each case it may be advantageous to isolate or synthesise the biologically more active isomer, where the individual components have different biological activity.

The compound of formulae (I) to (IX) may also be obtained in the form of their hydrates and/or may include other solvents, for example solvents that may have been used for the crystallisation of compounds in solid form.

10

The invention relates to all those embodiments of the process according to which a compound obtainable as starting material or intermediate at any stage of the process is used as starting material and some or all of the remaining steps are carried out or a starting material is used in the form of a derivative or salt and/or diastereoisomers, or, especially, is  
15 formed under the reaction conditions. For instance a compound of formula (I) can be used as a starting material for the preparation of another compound of formula (I). Such manipulation methods are known to those skilled in the art.

20 In the processes of the present invention it is preferable to use those starting materials and intermediates, which result in a compound of formula (I).

The invention relates especially to the preparation processes described in Examples P1 to P30.

25 Also within the scope of the present invention is a compound of formula (I) having a protecting group on the oxygen atom at the 5-carbon position instead of being a hydroxy group. In the event the protecting group is hydrolysable under mild conditions (such protecting groups include, for example unsubstituted or mono- to pentasubstituted



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C<sub>1</sub>-C<sub>12</sub>alkylcarbonates) or is a hydrocarbyl or substituted derivative thereof (such as, a unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl, in which one or more carbon atoms can be replaced by one or more oxygen atoms).

- 5 The compounds of formulae (II) to (VIII) also form part of the present invention. The compounds of formulae (II) to (VIII) may have either a protecting group on the oxygen atom at the 5-carbon position, or alternatively are deprotected, preferably each has a protecting group to protect the oxygen atom at the 5-carbon position. In the event, compounds of formulae (IV), (VI), (VII) and (VIII) are deprotected and a hydroxy group is bound to the 5-  
10 carbon position, such compounds are within the scope of formula (I).

- Compounds of formulae (III) and (V) in a protected or unprotected form also show pesticidal activity, especially in the event where the protecting group is not present (*i.e.*, hydroxy group at the 5-carbon position) or where the protecting group is hydrolysable under  
15 mild conditions (such protecting groups include, for example unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkylcarbonate).

- The compounds of the formulae (II) to (VIII), in particular (III) and (V), in both the protected and deprotected form are intermediates for the synthesis of compounds of formula (I). The  
20 use, therefore, of compounds of formula (II) to (VIII) in both the protected and deprotected form for the synthesis of compounds of formula (I) is also a subject of this invention. The preferences for the substituent groups, as appropriate, are the same as defined for the compound of the formula (I) in groups (2) to (22).

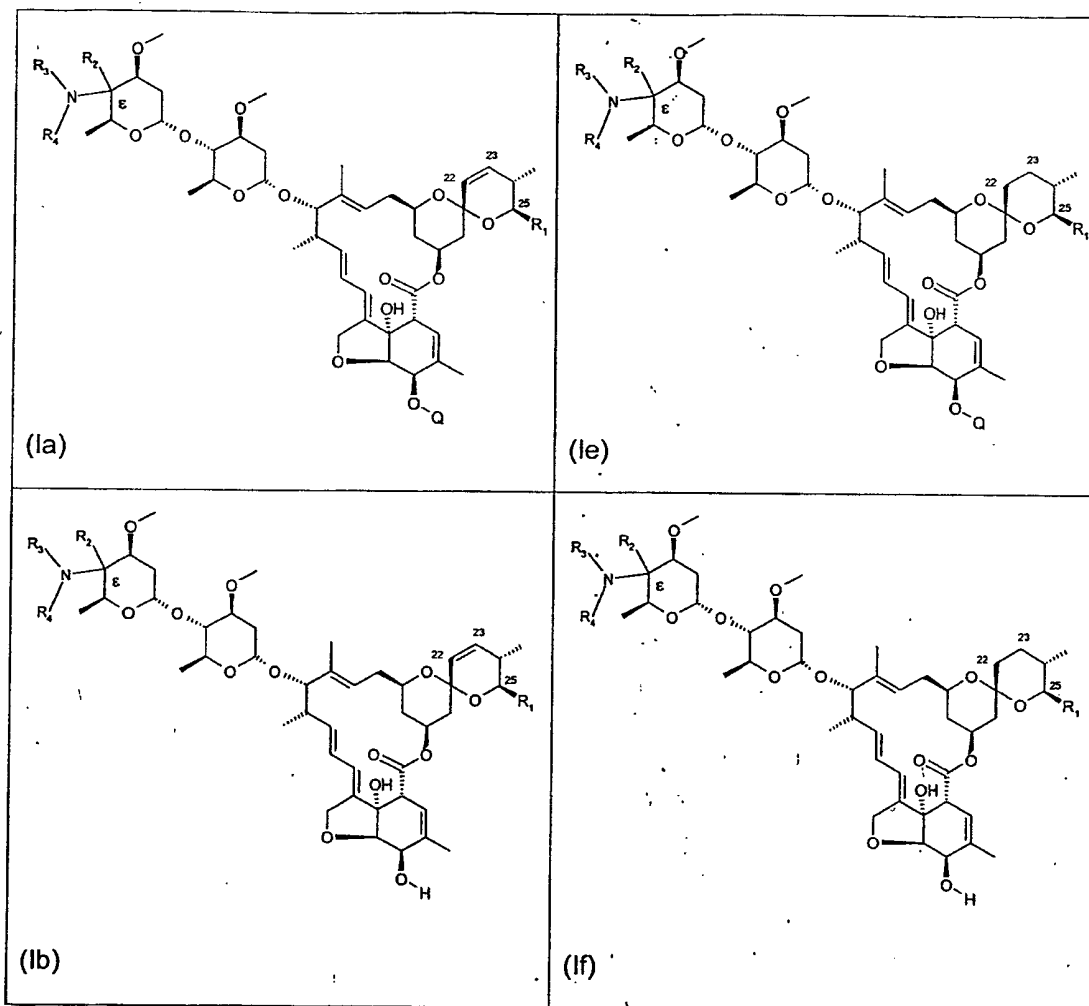
- 25 In the context of the invention, a reference is made to:

- compounds of formulae (Ia to Ih) of Table X and Tables 1 to 48;
- compounds of formulae (IIIa to IIId) of Table Y and Tables 49 to 72 ; and

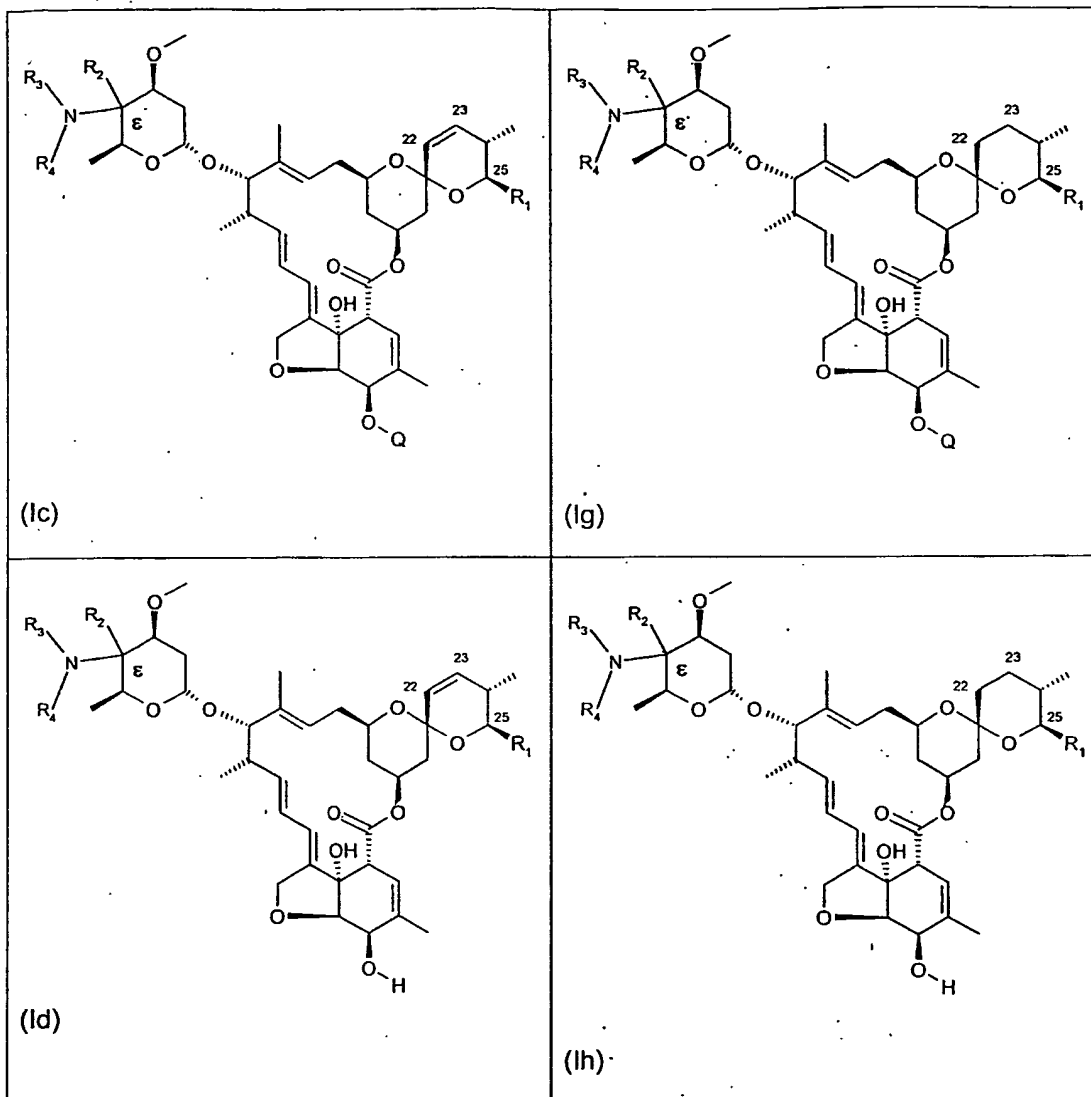
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- compounds of formulae (Va to Vd) of Table Z and Tables 73 to 96 ; and in each case, if appropriate, to its E / Z isomer or a mixture thereof.

Table X: A compound of any one of the formulae (Ia) to (Ih)



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where, for each formula

Line	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
1	CF <sub>3</sub>	OH	CH <sub>3</sub>
2	CF <sub>3</sub>	OH	Et
3	CF <sub>3</sub>	H	H
4	CF <sub>3</sub>	CH <sub>3</sub> C(O)	H
5	CF <sub>3</sub>	HC(O)	H

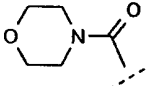
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Line	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
6	CF <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
7	CF <sub>3</sub>	CH <sub>3</sub> OC(O)	H
8	CF <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H
9	CF <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H
10	CF <sub>3</sub>	H	CH <sub>3</sub>
11	CF <sub>3</sub>	CH <sub>3</sub> C(O)	CH <sub>3</sub>
12	CF <sub>3</sub>	HC(O)	CH <sub>3</sub>
13	CF <sub>3</sub>	CH <sub>3</sub> OC(O)	CH <sub>3</sub>
14	CF <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	CH <sub>3</sub>
15	CF <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	CH <sub>3</sub>
16	CH <sub>3</sub> CH <sub>2</sub>	OH	CH <sub>3</sub>
17	CH <sub>3</sub> CH <sub>2</sub>	OH	Et
18	CH <sub>3</sub> CH <sub>2</sub>	H	H
19	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> C(O)	H
20	CH <sub>3</sub> CH <sub>2</sub>	HC(O)	H
21	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub>	CH <sub>3</sub>
22	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> OC(O)	H
23	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H
24	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H
25	CH <sub>3</sub> CH <sub>2</sub>	H	CH <sub>3</sub>
26	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> C(O)	CH <sub>3</sub>
27	CH <sub>3</sub> CH <sub>2</sub>	HC(O)	CH <sub>3</sub>
28	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> OC(O)	CH <sub>3</sub>
29	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	CH <sub>3</sub>
30	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	CH <sub>3</sub>
31	CH <sub>3</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> C(O)	
32	CF <sub>3</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> C(O)	
33	CH <sub>3</sub> CH <sub>2</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> C(O)	

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Line	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
34	Vinyl	C(O)CH <sub>2</sub> CH <sub>2</sub> C(O)	
35	Allyl	C(O)CH <sub>2</sub> CH <sub>2</sub> C(O)	
36	CH <sub>3</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
37	CF <sub>3</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
38	CH <sub>3</sub> CH <sub>2</sub>	C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
39	Vinyl	C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
40	Allyl	C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
41		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	H
42		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	C(O)CH <sub>3</sub>
43		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	C(O)H
44		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	C(O)CH <sub>2</sub> OCH <sub>3</sub>
45		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	C(O)OCH <sub>3</sub>
46		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>3</sub>
47		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>2</sub> CH <sub>3</sub>
48		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>2</sub> OCH <sub>3</sub>
49		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	CH <sub>2</sub> OCH <sub>2</sub> CH <sub>3</sub>
50		C(O)CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	SO <sub>2</sub> NH <sub>2</sub>
51	CH <sub>3</sub>	C(O)N(CH <sub>3</sub> ) <sub>2</sub>	H
52	CH <sub>3</sub>	C(O)N(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub>
53	CH <sub>3</sub>	C(S)CH <sub>3</sub>	H
54	CH <sub>3</sub>	C(S)CH <sub>3</sub>	CH <sub>3</sub>
55	CH <sub>3</sub>	S(O)Ph	H
56	CH <sub>3</sub>	S(O)Ph	CH <sub>3</sub>
57	CH <sub>3</sub>	S(O) <sub>2</sub> Ph	H
58	CH <sub>3</sub>	S(O) <sub>2</sub> Ph	CH <sub>3</sub>
59	CH <sub>3</sub>	CH <sub>2</sub> C(O)CH <sub>3</sub>	H
60	CH <sub>3</sub>	CH <sub>2</sub> C(O)CH <sub>3</sub>	CH <sub>3</sub>

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Line	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
61	CH <sub>3</sub>	CH <sub>2</sub> C(O)NH(CH <sub>3</sub> )	H
62	CH <sub>3</sub>	CH <sub>2</sub> C(O)NH(CH <sub>3</sub> )	CH <sub>3</sub>
63	CH <sub>3</sub>	CH <sub>2</sub> C(O)O CH <sub>3</sub>	H
64	CH <sub>3</sub>	CH <sub>2</sub> C(O)O CH <sub>3</sub>	CH <sub>3</sub>
65	CH <sub>3</sub>	CH <sub>3</sub> C(O)	CH <sub>3</sub>
66	CH <sub>3</sub>	HC(O)	CH <sub>3</sub>
67	CH <sub>3</sub>	CH <sub>3</sub> OC(O)	CH <sub>3</sub>
68	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	CH <sub>3</sub>
69	CH <sub>3</sub>	N(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub>
70	CN	CH <sub>2</sub> C(CH <sub>3</sub> )C(O)	CH <sub>3</sub>
71	CN	CH <sub>2</sub> CHC(O)	H
72	CN	(CH <sub>3</sub> ) <sub>2</sub> NC(O)	H
73	CN	CH <sub>3</sub> CHCHC(O)	H
74	CN	CH <sub>2</sub> CH(CH <sub>3</sub> )C(O)	H
75	CN	(CH <sub>3</sub> ) <sub>2</sub> NC(O)	H
76	CN	(CH <sub>3</sub> ) <sub>2</sub> CHC(O)	H
77	CN	cyclobutylC(O)	H
78	CN	CH <sub>3</sub> CH <sub>2</sub> SC(O)	H
79	CN		H

and

Table 1	A compound of the formula (Ia) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is ( <i>R</i> ), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 2	A compound of the formula (Ia) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is ( <i>S</i> ), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.

Table 3	A compound of the formula (Ia) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the ε position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 4	A compound of the formula (Ia) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the ε position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 5	A compound of the formula (Ia) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the ε position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 6	A compound of the formula (Ia) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the ε position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 7	A compound of the formula (Ib) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 8	A compound of the formula (Ib) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 9	A compound of the formula (Ib) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the ε position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 10	A compound of the formula (Ib) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the ε position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 11	A compound of the formula (Ib) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the ε position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 12	A compound of the formula (Ib) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the ε position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 13	A compound of the formula (Ic) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of

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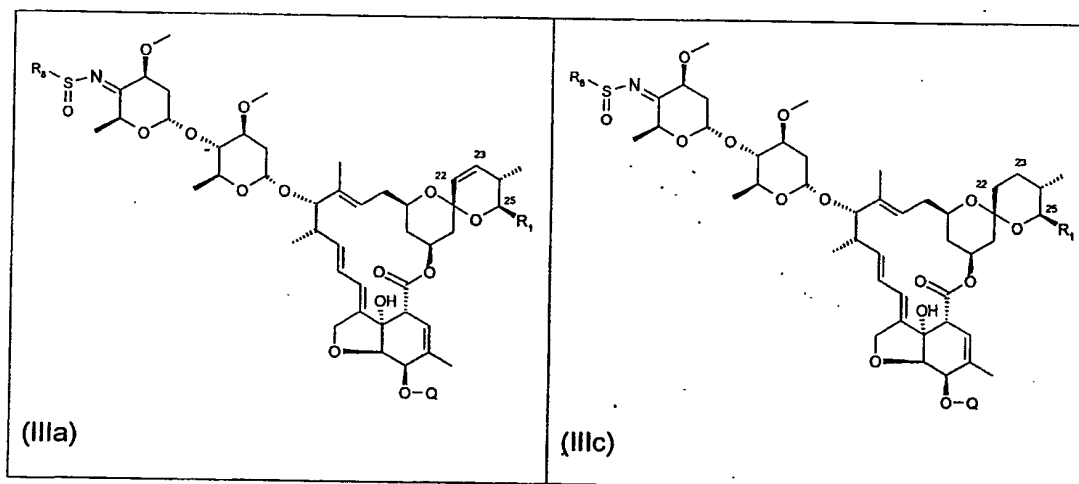
	the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 14	A compound of the formula (Ic) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>S</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 15	A compound of the formula (Ic) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 16	A compound of the formula (Ic) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>S</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 17	A compound of the formula (Ic) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 18	A compound of the formula (Ic) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>S</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 19	A compound of the formula (Id) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 20	A compound of the formula (Id) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>S</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 21	A compound of the formula (Id) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 22	A compound of the formula (Id) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>S</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 23	A compound of the formula (Id) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is ( <i>R</i> ), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a

	line 1 to 79 of Table X.
Table 24	A compound of the formula (Id) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 25	A compound of the formula (Ie) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 26	A compound of the formula (Ie) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 27	A compound of the formula (Ie) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 28	A compound of the formula (Ie) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 29	A compound of the formula (Ie) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 30	A compound of the formula (Ie) wherein R <sub>1</sub> is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 31	A compound of the formula (If) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 32	A compound of the formula (If) wherein R <sub>1</sub> is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.
Table 33	A compound of the formula (If) wherein R <sub>1</sub> is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents R <sub>2</sub> , R <sub>3</sub> and R <sub>4</sub> corresponds to a line 1 to 79 of Table X.

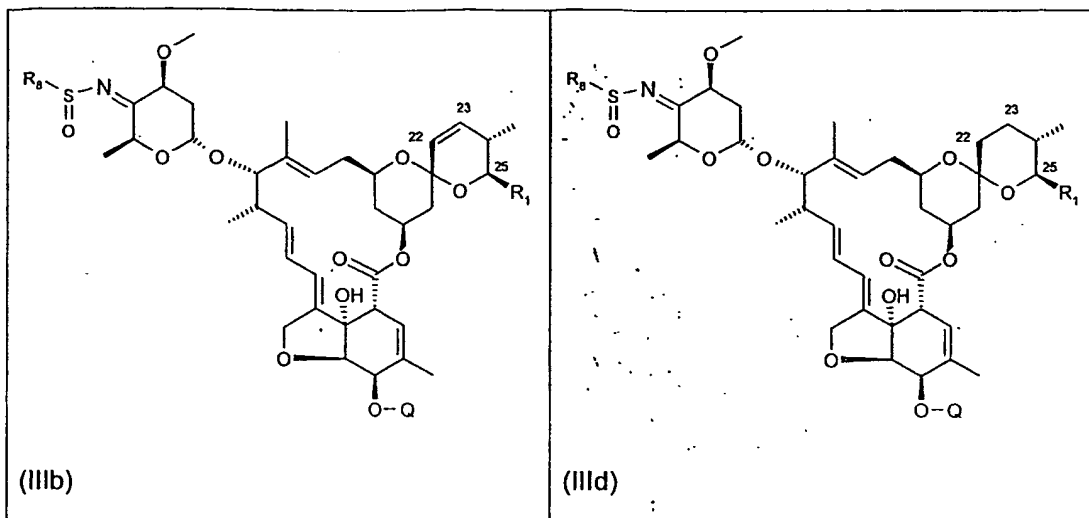
Table 34	A compound of the formula (If) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 35	A compound of the formula (If) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 36	A compound of the formula (If) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 37	A compound of the formula (Ig) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 38	A compound of the formula (Ig) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 39	A compound of the formula (Ig) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 40	A compound of the formula (Ig) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 41	A compound of the formula (Ig) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 42	A compound of the formula (Ig) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 43	A compound of the formula (Ih) wherein $R_1$ is sec-butyl or isopropyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 44	A compound of the formula (Ih) wherein $R_1$ is sec-butyl or isopropyl, the configuration of

	the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 45	A compound of the formula (Ih) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 46	A compound of the formula (Ih) wherein $R_1$ is cyclohexyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 47	A compound of the formula (Ih) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (R), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.
Table 48	A compound of the formula (Ih) wherein $R_1$ is 1-methyl butyl, the configuration of the carbon atom at the $\epsilon$ position is (S), and the substituents $R_2$ , $R_3$ and $R_4$ corresponds to a line 1 to 79 of Table X.

Table Y: A compound of any one of the formulae (IIIa to IIId)



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where

Line	R <sub>8</sub>	Q
1	Ph	SiMe <sub>2</sub> tBu
2	Ph	Me
3	Ph	C(O)CH <sub>3</sub>
4	Ph	CH <sub>2</sub> OCH <sub>3</sub>
5	Ph	C(O)OCH <sub>3</sub>
6	Ph	C(O)OCH <sub>2</sub> CHCH <sub>2</sub>

and

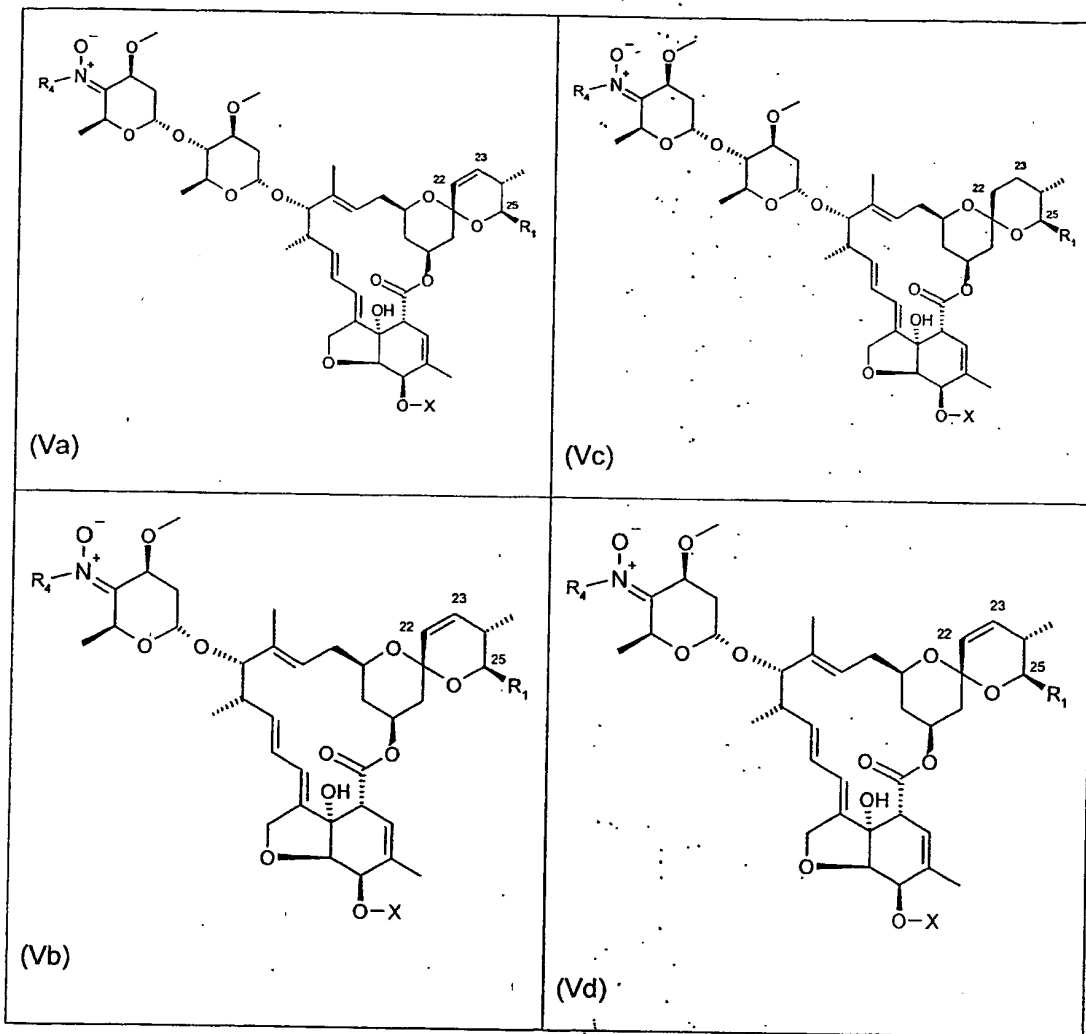
Table 49	A compound of the formula (IIIa) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 50	A compound of the formula (IIIa) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 51	A compound of the formula (IIIa) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the

	substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 52	A compound of the formula (IIIa) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 53	A compound of the formula (IIIa) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 54	A compound of the formula (IIIa) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 55	A compound of the formula (IIIb) wherein $R_1$ is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 56	A compound of the formula (IIIb) wherein $R_1$ is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 57	A compound of the formula (IIIb) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 58	A compound of the formula (IIIb) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 59	A compound of the formula (IIIb) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 60	A compound of the formula (IIIb) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.
Table 61	A compound of the formula (IIIc) wherein $R_1$ is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_8$ and Q corresponds to a line 1 to 6 of Table Y.

Table 62	A compound of the formula (IIIc) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 63	A compound of the formula (IIIc) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 64	A compound of the formula (IIIc) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 65	A compound of the formula (IIIc) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 66	A compound of the formula (IIIc) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 67	A compound of the formula (IIId) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 68	A compound of the formula (IIId) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 69	A compound of the formula (IIId) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 70	A compound of the formula (IIId) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 71	A compound of the formula (IIId) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>8</sub> and Q corresponds to a line 1 to 6 of Table Y.
Table 72	A compound of the formula (IIId) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration,

and the substituents  $R_8$  and Q corresponds to a line 1 to 6 of Table Y.

Table Z: A compound of any one of the formulae (Va to Vd)





where

Line	$R_4$	X
1	$CH_3$	$Si^tBu(CH_3)_2$



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Line	R <sub>4</sub>	X
2	CH <sub>3</sub>	H
3	PhCH <sub>2</sub>	Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
4	PhCH <sub>2</sub>	H
5	CH <sub>2</sub> CH CH <sub>2</sub>	Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
6	CH <sub>2</sub> CH CH <sub>2</sub>	H
7	CH <sub>3</sub> CH <sub>2</sub>	Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
8	CH <sub>3</sub> CH <sub>2</sub>	H
9	iPr	Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
10	iPr	H
11	tBu	Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
12	tBu	H
13		Si <sup>t</sup> Bu(CH <sub>3</sub> ) <sub>2</sub>
14		H

and

Table 73	A compound of the formula (Va) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 74	A compound of the formula (Va) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 75	A compound of the formula (Va) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.

Table 76	A compound of the formula (Va) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 77	A compound of the formula (Va) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 78	A compound of the formula (Va) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 79	A compound of the formula (Vb) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 80	A compound of the formula (Vb) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 81	A compound of the formula (Vb) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 82	A compound of the formula (Vb) wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 83	A compound of the formula (Vb) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 84	A compound of the formula (Vb) wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 85	A compound of the formula (Vc) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents R <sub>4</sub> and X corresponds to a line 1 to 14 of Table Z.
Table 86	A compound of the formula (Vc) wherein R <sub>1</sub> is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration,

	and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 87	A compound of the formula (Vc) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 88	A compound of the formula (Vc) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 89	A compound of the formula (Vc) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 90	A compound of the formula (Vc) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 91	A compound of the formula (Vd) wherein $R_1$ is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 92	A compound of the formula (Vd) wherein $R_1$ is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 93	A compound of the formula (Vd) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 94	A compound of the formula (Vd) wherein $R_1$ is cyclohexyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 95	A compound of the formula (Vd) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is E configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.
Table 96	A compound of the formula (Vd) wherein $R_1$ is 1-methyl butyl, the bond between the carbon atom at the 4' or 4'' position (as appropriate) and nitrogen atom is Z configuration, and the substituents $R_4$ and X corresponds to a line 1 to 14 of Table Z.

In the area of pest control, a compound of formula (I), (III) or (V) is an active compound (also referred to as active ingredient) exhibiting valuable preventive and/or curative activity with a very advantageous biocidal spectrum and a very broad spectrum, even at low rates of concentration, while being well tolerated by warm-blooded animals, fish and plants. They are, surprisingly, equally suitable for controlling both plant pests and ecto- and endo-parasites in humans and more especially in productive livestock, domestic animals and pets. They are effective against all or individual development stages of normally sensitive animal pests, but also of resistant animal pests, such as representatives of the class insecta, order Acarina, class nematoda, cestodes and trematodes, while at the same time protecting useful organisms. The insecticidal, acaricidal or nematocidal activity of the active ingredients according to the invention may manifest itself directly, *i.e.*, in the mortality of the pests, which occurs immediately or only after some time, for example during moulting, or indirectly, for example in reduced oviposition and/or hatching rate, good activity corresponding to a mortality of at least 50 to 60 %.

Successful control within the scope of the subject of the invention is possible, in particular, of pests from the orders Lepidoptera, Coleoptera, Orthoptera, Isoptera, Psocoptera, Anoplura, Mallophaga, Thysanoptera, Heteroptera, Homoptera, Hymenoptera, Diptera, Siphonaptera, Thysanura and Acarina, mainly Lepidoptera and Coleoptera. Very especially good control is possible of the following pests:

Abagrotis spp., Abraxas spp., Acantholeucania spp., Acanthoplusia spp., Acarus spp., Acarus siro, Aceria spp., Aceria sheldoni, Acleris spp., Acoloithus spp., Acompsia spp., Acossus spp., Acria spp., Acrobasis spp., Acrocercops spp., Acrolepia spp., Acrolepiopsis spp., Acronicta spp., Acropolitis spp., Actebia spp., Aculus spp., Aculus schlehtendali, Adoxophyes spp., Adoxophyes reticulana, Aedes spp., Aegeria spp., Aethes spp., Agapeta spp., Agonopterix spp., Agriopis spp., Agriotes spp., Agriphila spp., Agrochola spp., Agroperina spp., Alabama spp., Alabama argillaceae, Agrotis spp., Albuna spp., Alcathoe spp., Alcis spp., Aleimma spp., Aletia spp., Aleurothrixus spp., Aleurothrixus floccosus, Aleyrodes spp., Aleyrodes brassicae, Allophytes spp., Alsophila spp., Amata spp., Amathes

- spp., Amblyomma spp., Amblyptilia spp., Ammonoconia spp., Amorbia spp., Amphion spp., Amphipoea spp., Amphipyra spp., Amyeloides spp., Anacamptodes spp., Anagrapta spp., Anarsia spp., Anatrychytis spp., Anavitrinella spp., Ancylis spp., Andropolia spp., Anhimella spp., Antheraea spp., Antherigona spp., Antherigona soccata, Anthonomus spp.,
- 5 Anthonomus grandis, Anticarsia spp., Anticarsia gemmatilis, Aonidiella spp., Apamea spp., Aphania spp., Aphelia spp., Aphididae, Aphis spp., Apotomis spp., Aproaerema spp., Archippus spp., Archips spp., Acromyrmex, Arctia spp., Argas spp., Argolamprotes spp., Argyresthia spp., Argyrogramma spp., Argyroploce spp., Argyrotaenia spp., Arotrophora spp., Ascotis spp., Aspidiotus spp., Aspilapteryx spp., Asthenoptycha spp., Aterpia spp.,
- 10 Athetis spp., Atomaria spp., Atomaria linearis, Atta spp., Atypha spp., Autographa spp., Axylia spp., Bactra spp., Barbara spp., Batrachedra spp., Battaristis spp., Bembecia spp., Bemisia spp., Bemisia tabaci, Bibio spp., Bibio hortulanus, Bisigna spp., Blastesthia spp., Blatta spp., Blatella spp., Blepharosis spp., Bleptina spp., Boarmia spp., Bombyx spp., Bomolocha spp., Boophilus spp., Brachmia spp., Bradina spp., Brevipalpus spp., Brithys
- 15 spp., Bryobia spp., Bryobia praetiosa, Bryotropha spp., Bupalus spp., Busseola spp., Busseola fusca, Cabera spp., Cacoecimorpha spp., Cadra spp., Cadra cautella, Caenurgina spp., Calipitimerus spp., Callierges spp., Callophora spp., Callophora erythrocephala, Calophasia spp., Caloptilia spp., Calybites spp., Capnoptycha spp., Capua spp., Caradrina spp., Caripeta spp., Carmenta spp., Carposina spp., Carposina
- 20 nipponensis, Catamacta spp., Catelaphris spp., Catoptria spp., Caustoloma spp., Celaena spp., Celypha spp., Cenopsis spp., Cephus spp., Ceramica spp., Cerapteryx spp., Ceratitis spp., Ceratophyllus spp., Ceroplaster spp., Chaetocnema spp., Chaetocnema tibialis, Chamaesphesia spp., Charanva spp., Cheimophila spp., Chersotis spp., Chiasmia spp., Chilo spp., Chionodes spp., Chorioptes spp., Choristoneura spp., Chrysaspidia spp.,
- 25 Chrysodeixis spp., Chrysomya spp., Chrysomphalus spp., Chrysomphalus dictyospermi, Chrysomphalus aonidium, Chrysoteuchia spp., Cilix spp., Cimex spp., Clysia spp., Clysia ambiguella, Clepsia spp., Cnaemidophorus spp., Cnaphalocrocis spp., Cnephasia spp., Coccus spp., Coccus hesperidum, Cochylis spp., Coleophora spp., Colotois spp., Commophila spp., Conistra spp., Conopomorpha spp., Corcyra spp., Cornutiplusia spp.,
- 30 Cosmia spp., Cosmopolites spp., Cosmopterix spp., Cossus spp., Costaeonvexa spp., Crambus spp., Creatonotos spp., Crocidolomia spp., Crocidolomia binotalis, Croesia spp., Crymodes spp., Cryptaspa spp., Cryptoblabes spp., Cryptocala spp., Cryptophlebia spp., Cryptophlebia leucotreta, Cryptoptilia spp., Ctenopseustis spp., Cucullia spp., Curculio spp., Culex spp., Cuterebra spp., Cydia spp., Cydia pomonella, Cymbalophora spp.,

- Dactylethra spp., Dacus spp., Dadica spp., Damalinea spp., Dasychira spp., Decadarchis spp., Decodes spp., Deilephila spp., Deltodes spp., Dendrolimus spp., Depressaria spp., Dermestes spp., Dermanyssus spp., Dermanyssus gallinae, Diabrotica spp., Diachrysia spp., Diaphania spp., Diarsia spp., Diasemia spp., Diatraea spp., Diceratura spp.,
- 5 Dichomeris spp., Dichrocrocis spp., Dichrorampha spp., Dicycla spp., Dioryctria spp., Diparopsis spp., Diparopsis castanea, Dipleurina spp., Diprion spp., Diprionidae, Discestra spp., Distantiella spp., Distantiella theobroma, Ditula spp., Diurnea spp., Doratopteryx spp., Drepana spp., Drosophila spp., Drosophila melanogaster, Dysauxes spp., Dysdercus spp., Dysstroma spp., Eana spp., Earias spp., Ecclitica spp., Ecdytolopha spp., Ecpyrrhorhoe
- 10 spp., Ectomyelois spp., Eetropis spp., Egira spp., Elasmopalpus spp., Emmelia spp., mpoasca spp., Empyreuma spp., Enargia spp., Enarmonia spp., Endopiza spp., Endothenia spp., Endotricha spp., Eoreuma spp., Eotetranychus spp., Eotetranychus carpini, Epagoge spp., Epelis spp., Ephestia spp., Ephestiodes spp., Epiblema spp., Epiehoristodes spp., Epinotia spp., Epiphyas spp., Epiplema spp., Epipsestis spp., Epirrhoe
- 15 spp., Episimus spp., Epitymbia spp., Eplachna spp., Erannis spp., Erastria spp., Eremnus spp., Ereunetis spp., Eriophyes spp., Eriosoma spp., Eriosoma lanigerum, Erythroneura spp., Estigmene spp., Ethmia spp., Etiella spp., Euagrotis spp., Eucosma spp., Euehlaena spp., Euelidia spp., Eueosma spp., Euchistus spp., Eucosmomorpha spp., Eudonia spp., Eufidonia spp., Euhyponomeutoides spp., Eulepitodes spp., Eulia spp., Eulithis spp.,
- 20 Eupithecia spp., Euplexia spp., Eupoecilia spp., Eupoecilia ambiguella, Euproctis spp., Eupsilia spp., Eurhodope spp., Eurois spp., Eurygaster spp., Eurythmia spp., Eustrotia spp., Euxoa spp., Euzophera spp., Evergestis spp., Evippe spp., Exartema spp., Fannia spp., Faronta spp., Feltia spp., Filatima spp., Fishia spp., Frankliniella spp., Fumibotys spp., Gaesa spp., Gasgardia spp., Gastrophilus spp., Gelechia spp., Gilpinia spp., Gilpinia
- 25 polytoma, Glossina spp., Glyphipterix spp., Glyphodes spp., Gnorimoschemini spp., Gonodonta spp., Gortyna spp., Gracillaria spp., Graphania spp., Grapholita spp., Grapholitha spp., Gravitar mata spp., Gretchena spp., Griselda spp., Gryllotalpa spp., Gynaephora spp., Gypsonoma spp., Hada spp., Haematopinus spp., Halisidota spp., Harpieteryx spp., Harrisina spp., Hedyia spp., Helicoverpa spp., Heliophobus spp., Heliiothis
- 30 spp., Hellula spp., Helotropa spp., Hemaris spp., Hercinothrips spp., Herculia spp., Hermonassa spp., Heterogenea spp., Holomelina spp., Homadaula spp., Homoeosoma spp., Homoglaea spp., Homohadena spp., Homona spp., Homonopsis spp., Hoplocampa spp., Hoplodrina spp., Hoshinoa spp., Hxalomma spp., Hydraecia spp., Hydriomena spp., Hyles spp., Hyloicus spp., Hypagyrtis spp., Hypatima spp., Hyphantria spp., Hyphantria

- cunea, Hypocala spp., Hypocoena spp., Hypodema spp., Hyppobosca spp., Hypsipyla spp., Hyssia spp., Hysterosia spp., Idaea spp., Idia spp., Ipimorpha spp., Isia spp., Isochorista spp., Isophrictis spp., Isopolia spp., Isotrias spp., Ixodes spp., Itame spp., Jodia spp., Jodis spp., Kawabea spp., Keiferia spp., Keiferia lycopersicella, Labdia spp., Lacinipolia spp.,
- 5 Lambdina spp., Lamprothripa spp., Laodelphax spp., Lasius spp., Laspeyresia spp., Leptinotarsa spp., Leptinotarsa decemlineata, Leptocoris spp., Leptostales spp., Lecanium spp., Lecanium corni, Lepidosaphes spp., Lepisma spp., Lepisma saccharina, Lesmone spp., Leucania spp., Leucinodes spp., Leucophaea spp., Leucophaea maderae, Leucoptera spp., Leucoptera scitella, Linognathus spp., Liposcelis spp., Lissorhoptrus spp.,
- 10 Lithacodia spp., Lithocolletis spp., Lithomoia spp., Lithophane spp., Lixodessa spp., Lobesia spp., Lobesia botrana, Lobophora spp., Locusta spp., Lomanaltes spp., Lomographa spp., Loxagrotis spp., Loxostege spp., Lucilia spp., Lymantria spp., Lymnaecia spp., Lyonetia spp., Lyriomyza spp., Macdonnoughia spp., Macrauzata spp., Macronoctua spp., Macrosiphus spp., Malacosoma spp., Maliarpha spp., Mamestra spp., Mamestra
- 15 brassicae, Manduca spp., Manduca sexta, Marasmia spp., Margaritia spp., Matratinea spp., Matsumuraeses spp., Melanagromyza spp., Melipotes spp., Melissopus spp., Melittia spp., Melolontha spp., Meristis spp., Meritastis spp., Merophyas spp., Mesapamea spp., Mesogona spp., Mesoleuca spp., Metanema spp., Metendothenia spp., Metzneria spp., Micardia spp., Microcorses spp., Microleon spp., Mnesictena spp., Mocis spp., Monima
- 20 spp., Monochroa spp., Monomorium spp., Monomorium pharaonis, Monopsis spp., Morrisonia spp., Musca spp., Mutuuraia spp., Myelois spp., Mythimna spp., Myzus spp., Naranga spp., Nedra spp., Nemapogon spp., Neodiprion spp., Neosphaleroptera spp., Nephelodes spp., Nephrotettix spp., Nezara spp., Nilaparvata spp., Nipponympha spp., Nippoptilia spp., Noctua spp., Nola spp., Notocelia spp., Notodonta spp., Nudaurelia spp.,
- 25 Ochropleura spp., Ocnerostoma spp., Oestrus spp., Olethreutes spp., Oligia spp., Olindia spp., Olygonychus spp., Olygonychus gallinae, Oncomnemis spp., Operophtera spp., Ophisma spp., Opogona spp., Oraesia spp., Orniodoros spp., Orgyia spp., Oria spp., Orseolia spp., Orthodes spp., Orthogonia spp., Orthosia spp., Oryzaephilus spp., Oscinella spp., Oscinella frit, Osminia spp., Ostrinia spp., Ostrinia nubilalis, Otiorhynchus spp.,
- 30 Ourapteryx spp., Pachetra spp., Pachysphinx spp., Pagyda spp., Paleacrita spp., Paliga spp., Palthis spp., Pammene spp., Pandemis spp., Panemeria spp., Panolis spp., Panolis flammea, Panonychus spp., Paragyresthia spp., Paradiarsia spp., Paralobesia spp., Paranthrene spp., Parapandemis spp., Parapediasia spp., Parastichtis spp., Parasyndemis spp., Paratoria spp., Pareromeme spp., Pectinophora spp., Pectinophora gossypiella,

- Pediculus spp., Pegomyia spp., Pegomyia hyoscyami, Pelochrista spp., Pennisetia spp., Penstemonia spp., Pemphigus spp., Peribatodes spp., Peridroma spp., Perileucoptera spp., Periplaneta spp., Perizoma spp., Petrova spp., Pexicopia spp., Phalonia spp., Phalonidia spp., Phaneta spp., Phlyctaenia spp., Phlyctinus spp., Phorbia spp.,
- 5 Phragmatobia spp., Phricanthes spp., Phthorimaea spp., Phthorimaea operculella, Phyllocnistis spp., Phyllocoptruta spp., Phyllocoptruta oleivora, Phyllonorycter spp., Phyllophila spp., Phylloxera spp., Pieris spp., Pieris rapae, Piesma spp., Planococcus spp., Planotortrix spp., Platyedra spp., Platynota spp., Platyptilia spp., Platysenta spp., Plodia spp., Plusia spp., Plutella spp., Plutella xylostella, Podosesia spp., Polia spp., Popillia spp.,
- 10 Polymixis spp., Polyphagotarsonemus spp., Polyphagotarsonemus latus, Prays spp., Prionoxystus spp., Probole spp., Proceras spp., Prochoerodes spp., Proeulia spp., Proschistis spp., Proselena spp., Proserpinus spp., Protagrotis spp., Proteoteras spp., Protobathra spp., Protoschinia spp., Pselonophorus spp., Pseudaletia spp., Pseudanthonomus spp., Pseudaternalia spp., Pseudaulacaspis spp., Pseudexentera spp.,
- 15 Pseudococcus spp., Pseudohermenias spp., Pseudoplusia spp., Psoroptes spp., Psylla spp., Psylliodes spp., Pterophorus spp., Ptycholoma spp., Pulvinaria spp., Pulvinaria aethiopica, Pyralis spp., Pyrausta spp., Pyrgotis spp., Pyrreferra spp., Pyrrharctia spp., Quadraspidotus spp., Rancora spp., Raphia spp., Reticulitermes spp., Retinia spp., Rhagoletis spp., Rhagoletis pomonella, Rhipicephalus spp., Rhizoglyphus spp., Rhizopertha
- 20 spp., Rhodnius spp., Rhopalosiphum spp., Rhopobota spp., Rhyacia spp., Rhyacionia spp., Rhynchopacha spp., Rhyzosthenes spp., Rivula spp., Rondotia spp., Rusidrina spp., Rynchaglaea spp., Sabulodes spp., Sahlbergella spp., Sahlbergella singularis, Saissetia spp., Samia spp., Sannina spp., Sanninoidea spp., Saphoideus spp., Sarcoptes spp., Sathrobrotia spp., Scarabeidae, Sceliodes spp., Schinia spp., Schistocerca spp., Schizaphis
- 25 spp., Schizura spp., Schreckensteiniia spp., Sciara spp., Scirpophaga spp., Scirthraps auranti, Scoparia spp., Scopula spp., Scotia spp., Scotinophara spp., Scotogramma spp., Scrobipalpa spp., Scrobipalpopsis spp., Semiothisa spp., Sereda spp., Sesamia spp., Sesia spp., Sicya spp., Sideridis spp., Simyra spp., Sineugraphe spp., Sitochroa spp., Sitobion spp., Sitophilus spp., Sitotroga spp., Solenopsis spp., Smierinthus spp., Sophronia spp.,
- 30 Spaelotis spp., Spargaloma spp., Sparganothis spp., Spatalistis spp., Sperchia spp., Sphecia spp., Sphinx spp., Spilonota spp., Spodoptera spp., Spodoptera littoralis, Stigmatophora spp., Staphylinochrous spp., Stathmopoda spp., Stenodes spp., Sterraha spp., Stomoxys spp., Strophedra spp., Sunira spp., Sutyna spp., Swammerdamia spp., Syllomatia spp., Sympistis spp., Synanthedon spp., Synaxis spp., Syncopacma spp.,



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Syndemis spp., Syngrapha spp., Synthomeida spp., Tabanus spp., Taeniarchis spp.,  
 Taeniothrips spp., Tannia spp., Tarsonemus spp., Tegulifera spp., Tehama spp., Teleiodes  
 spp., Telorta spp., Tenebrio spp., Tephрина spp., Teratoglaea spp., Terricula spp., Tethea  
 spp., Tetranychus spp., Thalpophila spp., Thaumetopoea spp., Thiodia spp., Thrips spp.,  
 5 Thrips palmi, Thrips tabaci, Thyridopteryx spp., Thyris spp., Tineola spp., Tipula spp.,  
 Tortricidia spp., Tortrix spp., Trachea spp., Trialeurodes spp., Trialeurodes vaporariorum,  
 Triatoma spp., Triaxomera spp., Tribolium spp., Tricodectes spp., Trichoplusia spp.,  
 Trichoplusia ni, Trichoptilus spp., Trioza spp., Trioza erytreae, Triphaenia spp., Triphosa  
 spp., Trogoderma spp., Tyria spp., Udea spp., Unaspis spp., Unaspis citri, Uthetisa spp.,  
 10 Valeriodes spp., Vespa spp., Vespamima spp., Vitacea spp., Vitula spp., Witlesia spp.,  
 Xanthia spp., Xanthorhoe spp., Xanthotype spp., Xenomicta spp., Xenopsylla spp.,  
 Xenopsylla cheopsis, Xestia spp., Xylena spp., Xylomyges spp., Xyrosaris spp.,  
 Yponomeuta spp., Ypsolopha spp., Zale spp., Zanclognathus spp., Zeiraphera spp.,  
 Zenodoxus spp., Zeuzera spp., Zygaena spp.,

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It is also possible to control pests of the class Nematoda using the compounds according to  
 the invention. Such pests include, for example,

root knot nematodes, cyst-forming nematodes and also stem and leaf nematodes;

especially of Heterodera spp., e.g., Heterodera schachtii, Heterodera avenae and  
 20 Heterodera trifolii; Globodera spp., e.g. Globodera rostochiensis; Meloidogyne spp., e.g.,  
 Meloidogyne incognita and Meloidogyne javanica; Radopholus spp., e.g., Radopholus  
 similis; Pratylenchus, e.g., Pratylenchus neglectans and Pratylenchus penetrans;  
 Tylenchulus, e.g., Tylenchulus semipenetrans; Longidorus, Trichodorus, Xiphinema,  
 Ditylenchus, Apheenchoides and Anguina; especially Meloidogyne, e.g., Meloidogyne  
 25 incognita, and Heterodera, e.g., Heterodera glycines.

An especially important aspect of the present invention is the use of the compound of  
 formula (I), (III) or (V) in the protection of plants against parasitic feeding pests.

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The action of the compound of formula (I), (III) or (V) and the compositions comprising the said compound against animal pests can be significantly broadened and adapted to the given circumstances by the addition of other insecticides, acaricides or nematocides.

Suitable additives include, for example, representatives of the following classes of active ingredient: organophosphorus compounds, nitrophenols and derivatives, formamidines, uréas, carbamates, pyrethroids, chlorinated hydrocarbons, neonicotinoids and *Bacillus thuringiensis* preparations.

Examples of especially suitable mixing partners include: azamethiphos; chlorfenvinphos; cypermethrin, cypermethrin high-cis; cyromazine; diafenthiuron; diazinon; dichlorvos; dicrotophos; dicyclanil; fenoxycarb; fluazuron; furathiocarb; isazofos; iodfenphos; kinoprene; lufenuron; methacriphos; methidathion; monocrotophos; phosphamidon; profenofos; diofenolan; a compound obtainable from the *Bacillus thuringiensis* strain GC91 or from strain NCTC11821; pymetrozine; bromopropylate; methoprene; disulfoton; quinalphos; tau-fluvalinate; thiocyclam; thiometon; aldicarb; azinphos-methyl; benfuracarb; bifenthrin; buprofezin; carbofuran; dibutylaminothio; cartap; chlorfluazuron; chlorpyrifos; cyfluthrin; lambda-cyhalothrin; alpha-cypermethrin; zeta-cypermethrin; deltamethrin; diflubenzuron; endosulfan; ethiofencarb; fenitrothion; fenobucarb; fenvalerate; formothion; methiocarb; heptenophos; imidacloprid; thiamethoxam; clothianidine; isoprocarb; methamidophos; methomyl; mevinphos; parathion; parathion-methyl; phosalone; pirimicarb; propoxur; teflubenzuron; terbufos; triazamate; fenobucarb; tebufenozide; fipronil; beta-cyfluthrin; silafluofen; fenpyroximate; pyridaben; fenazaquin; pyriproxyfen; pyrimidifen; nitenpyram; acetamiprid; abamectin; emamectin; emamectin-benzoate; spinosad; a plant extract that is active against insects; a preparation that comprises nematodes and is active against insects; a preparation obtainable from *Bacillus subtilis*; a preparation that comprises fungi and is active against insects; a preparation that comprises viruses and is active against insects; chlorfenapyr; acephate; acrinathrin; alanycarb; alphamethrin; amitraz; AZ 60541; azinphos A; azinphos M; azocyclotin; bendiocarb; bensultap; beta-cyfluthrin; BPMC; brofenprox; bromophos A; bufencarb; butocarboxin; butylpyridaben; cadusafos; carbaryl; carbophenothion; chloethocarb; chlorethoxyfos; chlormephos; cis-resmethrin; clocythrin; clofentezine; cyanophos; cycloprothrin; cyhexatin; demeton M; demeton S; demeton-S-methyl; dichlofenthion; dicliphos; diethion; dimethoate; dimethylvinphos; dioxathion; edifenphos; esfenvalerate; ethion; ethofenprox; ethoprophos; etrimphos; fenamiphos;

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- fenbutatin oxide; fenothiocarb; fenpropathrin; fenpyrad; fenthion; fluazinam; flucycloxuron; flucythrinate; flufenoxuron; flufenprox; fonophos; fosthiazate; fubfenprox; HCH; hexaflumuron; hexythiazox; IKI-220; iprobenfos; isofenphos; isoxathion; ivermectin; malathion; mecarbam; mesulfenphos; metaldehyde; metolcarb; milbernecitin; moxidectin; naled; NC 184; omethoate; oxamyl; oxydemethon M; oxydeprofos; permethrin; phenthoate; phorate; phosmet; phoxim; pirimiphos M; pirimiphos E; promecarb; propaphos; prothiofos; prothoate; pyrachlophos; pyradaphenthion; pyresmethrin; pyrethrum; tebufenozide; salithion; sebufos; sulfotep; sulprofos; tebufenpyrad; tebupirimphos; tefluthrin; temephos; terbam; tetrachlorvinphos; thiacloprid; thiafenox; thiodicarb; thiofanox; thionazin; thuringiensin; tralomethrin; triarthene; triazophos; triazuron; trichlorfon; triflumuron; trimethacarb; vamidothion; xylylcarb; YI 5301/5302; zetamethrin; DPX-MP062 — indoxacarb; methoxyfenozide; bifenazate; XMC (3,5-xylyl methylcarbamate); or the fungus pathogen *Metarhizium anisopliae*.
- 15 A compound of formula (I), (III) or (V) can be used to control, *i.e.*, to inhibit or destroy, pests of the mentioned type occurring on plants, especially on useful plants and ornamentals in agriculture, in horticulture and in forestry, or on parts of such plants, such as the fruits, blossoms, leaves, stems, tubers or roots, while in some cases plant parts that grow later are still protected against those pests.
- 20
- Target crops include especially cereals, such as wheat, barley, rye, oats, rice, maize and sorghum; beet, such as sugar beet and fodder beet; fruit, *e.g.*, pomes, stone fruit and soft fruit, such as apples, pears, plums, peaches, almonds, cherries and berries, *e.g.*, strawberries, raspberries and blackberries; leguminous plants, such as beans, lentils, peas and soybeans; oil plants, such as rape, mustard, poppy, olives, sunflowers, coconut, castor oil, cocoa and groundnuts; cucurbitaceae, such as marrows, cucumbers and melons; fibre plants, such as cotton, flax, hemp and jute; citrus fruits, such as oranges, lemons, grapefruit and mandarins; vegetables, such as spinach, lettuce, asparagus, cabbages, carrots, onions, tomatoes, potatoes and paprika; lauraceae, such as avocado, cinnamon and camphor; and tobacco, nuts, coffee, aubergines, sugar cane, tea, pepper, vines, hops, bananas, natural rubber plants and ornamentals.

Further areas of use of a compound of formula (I), (III) or (V) is the protection of stored goods and storerooms and the protection of raw materials, and also in the hygiene sector, especially the protection of domestic animals and productive livestock against pests of the mentioned type, more especially the protection of domestic animals, especially cats and dogs, from infestation by fleas, ticks and nematodes.

The invention therefore relates also to a pesticidal composition, such as emulsifiable concentrates, suspension concentrates, directly sprayable or dilutable solutions, spreadable pastes, dilute emulsions, wettable powders, soluble powders, dispersible powders, wettable powders, dusts, granules and encapsulations of polymer substances, that comprises at least one compound of formula (I), (III) or (V), the choice of formulation being made in accordance with the intended objectives and the prevailing circumstances. Furthermore, the pesticidal composition is often diluted, and optionally combined with other pesticidal compositions, before its use as a pesticide. The invention, therefore, also relates to a tank mix composition (sometimes referred to as a slurry in the event the composition is a suspension), which comprises the pesticidal composition and a liquid carrier, generally water, and optionally one or more other pesticidal compositions, each other pesticidal composition comprising a further pesticide as active compound.

20

The active ingredient is used in those compositions in pure form, a solid active ingredient, for example, in a specific particle size, or preferably together with at least one of the auxiliary (also known as adjuvants) customary in formulation technology, such as extenders, e.g., solvents or solid carriers, or surface-active compounds (surfactants). In the area of parasite control in humans, domestic animals, productive livestock and pets it will be self-evident that only physiologically tolerable additives are used.

Solvents are, for example: non-hydrogenated or partly hydrogenated aromatic hydrocarbons, preferably fractions C<sub>8</sub> to C<sub>12</sub> of alkylbenzenes, such as xylene mixtures, alkylated naphthalenes or tetrahydronaphthalene, aliphatic or cycloaliphatic hydrocarbons,

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such as paraffins or cyclohexane, alcohols, such as ethanol, propanol or butanol, glycols and ethers and esters thereof, such as propylene glycol, dipropylene glycol ether, ethylene glycol or ethylene glycol monomethyl or -ethyl ether, ketones, such as cyclohexanone, isophorone or diacetone alcohol, strongly polar solvents, such as N-methylpyrrolid-2-one, dimethyl sulfoxide or N,N-dimethylformamide, water, non-epoxidized or epoxidized plant oils, such as non-epoxidized or epoxidized rapeseed, castor, coconut or soya oil, and silicone oils.

The solid carriers used, for example, for dusts and dispersible powders, are as a rule natural rock powders, such as calcite, talc, kaolin, montmorillonite or attapulgite. Highly disperse silicic acids or highly disperse absorbent polymers can also be added to improve the physical properties. Granular adsorptive granule carriers are porous types, such as pumice, crushed brick, sepiolite or bentonite, and non-sorbent carrier materials are calcite or sand. A large number of granular materials of inorganic or organic nature can furthermore be used, in particular dolomite or comminuted plant residues.

Surface-active compounds are, depending on the nature of the active compound to be formulated, nonionic, cationic and/or anionic surfactants or surfactant mixtures with good emulsifying, dispersing and wetting properties. The surfactants listed below are to be regarded only as examples; many other surfactants that are customary in formulation technology are suitable and are described in the relevant literature.

Nonionic surfactants are, in particular, polyglycol ether derivatives of aliphatic or cycloaliphatic alcohols, saturated or unsaturated fatty acids and alkylphenols, which can contain 3 to 30 glycol ether groups and 8 to 20 carbon atoms in the (aliphatic) hydrocarbon radical and 6 to 18 carbon atoms in the alkyl radical of the alkylphenols. Substances which are furthermore suitable are water-soluble polyethylene oxide adducts, containing 20 to 250 ethylene glycol ether and 10 to 100 propylene glycol ether groups, on propylene glycol, ethylene diaminopolypropylene glycol and alkyl polypropylene glycol having 1 to 10 carbon atoms in the alkyl chain. The compounds mentioned usually contain 1 to 5 ethylene glycol units per propylene glycol unit. Examples are nonylphenol-polyethoxyethanols, castor oil

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polyglycol ethers, polypropylene-polyethylene oxide adducts, tributylphenoxypolyethoxyethanol, polyethylene glycol and octylphenoxypolyethoxyethanol. Other substances are fatty acid esters of polyoxyethylene sorbitan, such as polyoxyethylene sorbitan trioleate.

- 5 The cationic surfactants are, in particular, quaternary ammonium salts which contain, as substituents, at least one alkyl radical having 8 to 22 C atoms and, as further substituents, lower, non-halogenated or halogenated alkyl, benzyl or lower hydroxyalkyl radicals. The salts are preferably in the form of halides, methyl-sulfates or ethyl-sulfates. Examples are stearyl-trimethyl-ammonium chloride and benzyl-di-(2-chloroethyl)-ethyl-ammonium  
10 bromide.

- Suitable anionic surfactants can be both water-soluble soaps and water-soluble synthetic surface-active compounds. Suitable soaps are the alkali metal, alkaline earth metal and substituted or unsubstituted ammonium salts of higher fatty acids ( $C_{10}$ - $C_{22}$ ), such as the  
15 sodium or potassium salts of oleic or stearic acid, or of naturally occurring fatty acid mixtures, which can be obtained, for example, from coconut oil or tall oil; and furthermore also the fatty acid methyl-taurine salts. However, synthetic surfactants are more frequently used, in particular fatty sulfonates, fatty sulfates, sulfonated benzimidazole derivatives or alkylarylsulfonates. The fatty sulfonates and sulfates are as a rule in the form of alkali  
20 metal, alkaline earth metal or substituted or unsubstituted ammonium salts and in general have an alkyl radical of 8 to 22 C atoms, alkyl also including the alkyl moiety of acyl radicals; examples are the sodium or calcium salt of ligninsulfonic acid, of dodecylsulfuric acid ester or of a fatty alcohol sulfate mixture prepared from naturally occurring fatty acids. These also include the salts of sulfuric acid esters and sulfonic acids of fatty alcohol-  
25 ethylene oxide adducts. The sulfonated benzimidazole derivatives preferably contain 2 sulfonic acid groups and a fatty acid radical having about 8 to 22 C atoms. Alkylarylsulfonates are, for example, the sodium, calcium or triethanolammonium salts of dodecylbenzenesulfonic acid, of dibutyl-naphthalenesulfonic acid or of a naphthalenesulfonic acid-formaldehyde condensation product. Corresponding phosphates, such as salts of the phosphoric acid ester of a p-nonylphenol-(4-14)-ethylene oxide adduct  
30 or phospholipids, can further also be used.

The compositions as a rule comprise 0.1 to 99 %, in particular 0.1 to 95 %, of active compound and 1 to 99.9 %, in particular 5 to 99.9 %, of at least one solid or liquid auxiliary, it being possible as a rule for 0 to 25 %, in particular 0.1 to 20 %, of the composition to be  
5 surfactants (% is in each case per cent by weight). While concentrated compositions are more preferred as commercial goods, the end user as a rule uses dilute compositions which comprise considerably lower concentrations of active compound. Preferred compositions are composed, in particular, as follows (% = per cent by weight):

10 Emulsifiable concentrates:

active ingredient:	1 to 90%, preferably 5 to 20%
surfactant:	1 to 30%, preferably 10 to 20%
solvent:	balance

15 Dusts:

active ingredient:	0.1 to 10%, preferably 0.1 to 1%
solid carrier:	99.9 to 90%, preferably 99.9 to 99%

Suspension concentrates:

20 active ingredient:	5 to 75%, preferably 10 to 50%
surfactant:	1 to 40%, preferably 2 to 30%
water:	balance



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Wettable powders:

active ingredient: 0.5 to 90%, preferably 1 to 80%

surfactant: 0.5 to 20%, preferably 1 to 15%

solid carrier: balance

5

Granules:

active ingredient: 0.5 to 30%, preferably 3 to 15%

solid carrier: 99.5 to 70%, preferably 97 to 85%

- 10 Specific formulation examples for use in crop protection are given below (% = per cent by weight):

Example F1: Emulsifiable concentrates

	a)	b)	c)
Active compound	25%	40%	50%
Calcium dodecylbenzenesulphonate	5%	8%	6%
Castor oil polyethylene glycol ether (36 mol of EO)	5%	-	-
Tributylphenol polyethylene glycol ether (30 mol of EO)	-	12%	4%
Cyclohexanone	-	15%	20%
Xylene mixture	65%	25%	20%

- 15 Mixing of finely ground active compound and additives gives an emulsion concentrate which, by dilution with water, affords emulsions of the desired concentration.

Example F2: Solutions

	a)	b)	c)	d)
Active compound	80%	10%	5%	95%
Ethylene glycol monomethyl ether	-	20%	-	-
Polyethylene glycol (MW 400)	-	70%	-	-
N-methylpyrrolid-2-one	20%	-	-	-
Epoxidized coconut oil	-	-	1%	-
Aliphatic hydrocarbon (boiling range: 160-190°)	-	-	94%	5%

Mixing of finely ground active compound and additives gives a solution suitable for use in the form of microdrops.

5 Example F3: Granules

	a)	b)	c)	d)
Active compound	5%	10%	8%	21%
Kaolin	94%	-	79%	54%
Finely divided silicic acid	1%	-	13%	7%
Attapulgate	-	90%	-	18%

The active compound is dissolved in dichloromethane, the solution is sprayed onto the mixture of carriers and the solvent is evaporated under reduced pressure.

Example F4: Wettable powder

	a)	b)	c)
Active compound	25%	50%	75%
Sodium lignosulphonate	5%	5%	-
Sodium lauryl sulphate	3%	-	5%
Sodium diisobutyl naphthalene sulphonate	-	6%	10%
Octylphenol polyethylene glycol ether (7-8 mol of EO)	-	2%	-
Finely divided silicic acid	5%	10%	10%
Kaolin	62%	27%	-

Active compound and additives are mixed and the mixture is ground in a suitable mill. This gives wettable powders which can be diluted with water to give suspensions of the desired concentration.

5

Example F5: Emulsifiable concentrate

Active compound	10%
Octylphenol polyethylene glycol ether (4-5 mol of EO)	3%
Calcium dodecylbenzenesulphonate	3%
Castor oil polyethylene glycol ether (36 mol of EO)	4%
Cyclohexanone	30%
Xylene mixture	50%

Mixing of finely ground active compound and additives gives an emulsion concentrate which, by dilution with water, affords emulsions of the desired concentration.

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Example F6: Extruder granules

Active compound	10%
Sodium lignosulphonate	2%
Carboxymethylcellulose	1%
Kaolin	87%

Active compound and additives are mixed, the mixture is ground, moistened with water, extruded and granulated, and the granules are dried in a stream of air.

5 Example F7: Coated granules

Active compound	3%
Polyethylene glycol (MW 200)	3%
Kaolin	94%

In a mixer, the finely ground active compound is applied uniformly to the kaolin which has been moistened with polyethylene glycol. This gives dust-free coated granules.

Example F8: Suspension concentrate

Active compound	40%
Ethylene glycol	10%
Nonylphenol polyethylene glycol ether (15 mol of EO)	6%
Sodium lignosulphonate	10%
Carboxymethylcellulose	1%
Aqueous formaldehyde solution (37%)	0.2%
Aqueous silicone oil emulsion (75%)	0.8%
Water	32%

- 10 Mixing of finely ground active compound and additives gives a suspension concentrate which, by dilution with water, affords suspensions of the desired concentration.

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The compositions according to the invention may also comprise further solid or liquid adjuvants, such as stabilisers, e.g., vegetable oils or epoxidised vegetable oils (e.g., epoxidised coconut oil, rapeseed oil or soybean oil), antifoams, e.g. silicone oil, preservatives, viscosity regulators, binders and/or tackifiers as well as fertilisers or other active ingredients for obtaining special effects, e.g., acaricides, bactericides, fungicides, nematocides, molluscicides or selective herbicides.

The pesticidal composition according to the invention, particularly for use as a crop protection product, is prepared in the absence of adjuvants, e.g., by grinding, sieving and/or compressing the compound of formula (I), (III) or (V) (as active ingredient) or mixture thereof, for example, to a certain particle size, and in the presence of at least one adjuvant, for example, by intimately mixing and/or grinding the compound of formula (I), (III) or (V) (as active ingredient) or mixture thereof with the adjuvant(s). The invention relates likewise to those processes for the preparation of the pesticidal composition according to the invention and to the use of a compound of formula (I), (III) or (V) in the preparation of the composition.

The invention relates also to the methods of application of the pesticidal and tank mix compositions, i.e., the methods of controlling pests of the mentioned type, such as spraying, atomising, dusting, coating, dressing, scattering or pouring, which are selected in accordance with the intended objectives and the prevailing circumstances, and to the use of the compositions for controlling pests of the mentioned type. Typical rates of concentration are from 0.1 to 1000 ppm, preferably from 0.1 to 500 ppm, of active ingredient. The rates of application per hectare are generally from 1 to 2000 g of active ingredient per hectare, especially from 10 to 1000 g/ha, preferably from 20 to 600 g/ha, most preferably from 20 to 100 g/ha.

A preferred method of application in the area of crop protection is application to the foliage of the plants (foliar application), the frequency and the rate of application being dependent upon the risk of infestation by the pest in question. However, the active ingredient can also penetrate the plants through the roots (systemic action) when the locus of the plants is

impregnated with a liquid formulation or when the active ingredient is incorporated in solid form into the locus of the plants, for example, into the soil, e.g., in granular form (soil application). In the case of paddy rice crops, such granules may be applied in metered amounts to the flooded rice field.

5

The pesticidal and tank mix compositions are also suitable for protecting plant propagation material, e.g., seed, such as fruits, tubers or grains, or plant cuttings, against animal pests. The propagation material can be treated with the composition before planting: seed, for example, can be dressed before being sown. The active ingredients according to the  
10 invention can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting site when the propagation material is being planted, for example, to the seed furrow during sowing. The invention relates also to such methods of treating plant propagation material and to the plant propagation material so treated.

15

#### Preparation Examples:

Since in most cases the compounds are present as mixtures of the avermectin derivatives B1a and B1b, characterization by customary physical data such as melting point or refractive index makes little sense. For this reason, the compounds are characterized by  
20 the retention times that are determined in an analysis by HPLC (high performance liquid chromatography). Here, the term B1a refers to the main component in which the group at position 25 ( $R_1$  in formula (I)) is sec-butyl, with a content of usually more than 80%. B1b denotes the minor component in which  $R_1$  is isopropyl. The compounds where two retention times are given both for the B1a and for the B1b derivative are mixtures of  
25 diastereoisomers, which can be separated chromatographically. In the case of compounds where a retention time is given only in column B1a or only in column B1b, the pure B1a or B1b component, respectively, can be obtained during work-up. The correct structures of the B1a and B1b components are assigned by mass spectrometry.

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The following methods are used for HPLC analysis:

**Method A (Water Alliance HT 2795)**

HPLC gradient conditions			
Solvent A:	0.01% of acid formic in H <sub>2</sub> O / CH <sub>3</sub> CN (1 : 1)		
Solvent B:	0.01% of acid formic in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	100	0	1.7
2.5	0	100	1.7
2.8	0	100	1.7
2.9	100	0	1.7
Type of column	Water atlantis dc18		
Column length	20 mm		
Internal diameter of column:	3 mm		
Particle Size:	3 micron		
Temperature	40°C		

**Method Z (Agilent HP1100)**

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H <sub>2</sub> O		
Solvent B:	0.01% of trifluoroacetic acid in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		

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Particle Size:	3.5 micron
Temperature	40°C

**Method Y (Agilent HP1100)**

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H <sub>2</sub> O		
Solvent B:	0.01% of trifluoroacetic acid in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	60	40	0.5
6	40	60	0.5
11	15	85	0.5
15	15	85	0.5
17	0	100	0.5
20	0	100	0.5
20.1	80	20	0.5
25	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		
Particle Size:	3.5 micron		
Temperature	40°C		

**Method X (Waters Alliance 2690)**

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H <sub>2</sub> O		
Solvent B:	0.01% of trifluoroacetic acid in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5



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14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		
Particle Size:	3.5 micron		
Temperature	40°C		

**Method W (Waters Alliance 2690)**

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H <sub>2</sub> O		
Solvent B:	0.01% of trifluoroacetic acid in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	50	50	0.5
10	5	95	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	YMC-Pack ODS-AQ		
Column length	125 mm		
Internal diameter of column:	2.0 mm		
Particle Size:	5 micron		
Temperature	40°C		

**Method V (Waters Alliance 2690)**

HPLC gradient conditions	
Solvent A:	0.01% of trifluoroacetic acid in H <sub>2</sub> O

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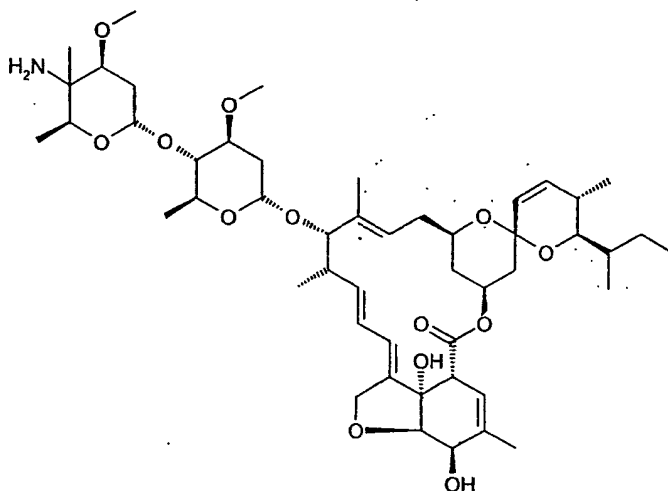
Solvent B:	0.01% of trifluoroacetic acid in CH <sub>3</sub> CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	YMC-Pack ODS-AQ		
Column length	125 mm		
Internal diameter of column:	2.0 mm		
Particle Size:	5 micron		
Temperature	40°C		

The particular method used for HPLC analysis is indicated in the column headed "LC-MS" in Tables A to L by the letters A, Z, Y, X, W and V, as appropriate.

- In the following examples, the mixing ratios of the eluents are given as volume/volume, and the temperatures in °C. Further, for simplicity, representation of the formula in the examples indicates the main derivative (B1a). TBDMS means *tert*-butyldimethylsilyl.

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Example P1: 4''-(R)-4''-desoxy-4''- amino-4''-methyl Avermectin B<sub>1</sub> and 4''-(S)-4''-desoxy-4''- amino-4''-methyl Avermectin B<sub>1</sub>



Step A: To a solution of 40 g of 5-OTBDMS-4''-desoxy-4''-hydroxyimino-avermectin B<sub>1</sub> and 20.3 g of diphenyl disulfide in 400 ml tetrahydrofuran at 0°C is added 23 ml of tributylphosphine. The mixture is stirred at 0°C for 1 hour. To the reaction mixture is added 80g of N-phenylmaleimide and the mixture is stirred at room temperature for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate, extracted with dichloromethane, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with hexane/diethyl ether to afford 5-OTBDMS-4''-desoxy-4''-phenylsulfenimine-Avermectin B<sub>1</sub>.

Step B: To a solution of 20 g 5-OTBDMS-4''-desoxy-4''-phenylsulfenimine-Avermectin B<sub>1</sub> (obtained in step A) in a mixture of 300 ml chloroform and 100 ml of saturated solution of sodium hydrogencarbonate at 0°C is added 5.9 g of m-chloroperbenzoic acid, and the mixture is stirred at 0°C for 45 minutes, poured into a aqueous saturated sodium hydrogencarbonate, extracted with dichloromethane; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford 5-OTBDMS-4''-desoxy-4''-phenylsulfinimine-Avermectin B<sub>1</sub>.

Step C: To a solution of 5-OTBDMS-4''-desoxy-4''-phenylsulfinimine-Avermectin B<sub>1</sub> (obtained in step B) in 360 ml of diethylether at 0°C is added 16.2 ml of methylmagnesium chloride (3M) and the mixture is stirred at 0°C for 30 minutes, then the ice bath is removed. 4 ml of methylmagnesium chloride (3M) is added to the solution at RT, and the mixture is

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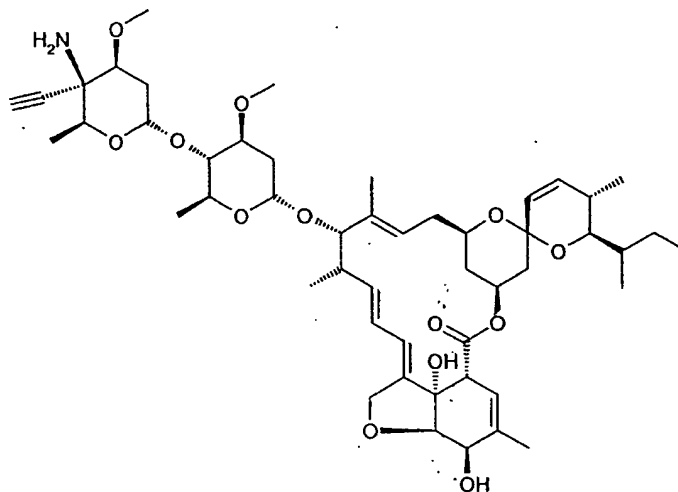
stirred at room temperature for 10 minutes, poured into a saturated sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford a mixture of 5-OTBDMS-4"-desoxy-4"-phenylsulfonamide-4"-methyl-Avermectin B<sub>1</sub>.

- 5 Step D: To a solution of 1.2 g 5-OTBDMS-4"-desoxy-4"-phenylsulfonamide-4"-methyl-Avermectin B<sub>1</sub> (obtained in step C) in 65 ml of dichloromethane at 0°C is added 0.46 ml of isopropanol and 0.46 ml of trifluoroacetic acid and the mixture is stirred at 0°C for 1 hour, poured into a mixture of saturated sodium hydrogencarbonate and brine (1:1), extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in*  
10 *vacuo* to afford a mixture of 5-OTBDMS-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub>. The residue is purified by chromatography on silica gel with hexane/ethylacetate to afford 5-OTBDMS-4"-(S)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub> and 5-OTBDMS-4"-(R)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub>.

- Step E: 0.691 g of 5-OTBDMS-4"-(S)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub> or 5-  
15 OTBDMS-4"-(R)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub> are dissolved in 17.5 ml tetrahydrofuran, then 3.5 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents  
20 are distilled off. The residue is purified by chromatography on silica gel with dichloromethane/methanol, yielding 4"-(S)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub> or 4"-(R)-4"-desoxy-4"-amino-4"-methyl-Avermectin B<sub>1</sub>.

Example P2: 4"-(R)-4"-desoxy-4"-amino-4"-ethynyl-Avermectin B<sub>1</sub>

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Step A: To a solution of 5-OTBDMS-4''-desoxy-4''-phenylsulfinimine-Avermectin B<sub>1</sub> (P1: Steps A and B) in 210 ml of tetrahydrofuran at -78°C is added 10.8 ml of trimethylsilylethynyl lithium salt (prepared in THF by action of butyllithium on

5 trimethylsilylacetylen) and the mixture is stirred at -78°C for 20 minutes, poured into a mixture of saturated sodium chloride and ethylacetate, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford a mixture of 5-OTBDMS-4''-(R)- 4''-desoxy-4''-phenylsulfinamide-4''-trimethylsilylethynyl-Avermectin B<sub>1</sub>.

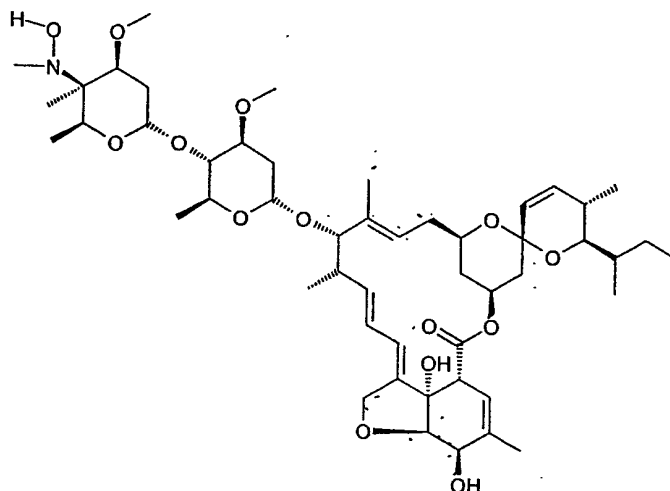
Step B: 5-OTBDMS-4''-(R)- 4''-desoxy-4''-phenylsulfinamide-4''-trimethylsilylethynyl-Avermectin B<sub>1</sub> (obtained from the step (A)) in methanol (60 ml) at 0 °C is added

10 methanesulphonic acid (3 ml). The reaction mixture is stirred for 1 hour and poured into saturated sodium bicarbonate, extracted with ethylacetate, dried over Mg<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. Flash chromatography (silica gel, hexane/ethylacetate 1/1) affords 4''-(R)- 4''-desoxy-4''-amino-4''-ethynyl-Avermectin B.

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Example P3: 4''-(R)- 4''-desoxy-4''-N-methyl hydroxylamino-4''-methyl -Avermectin B<sub>1</sub>

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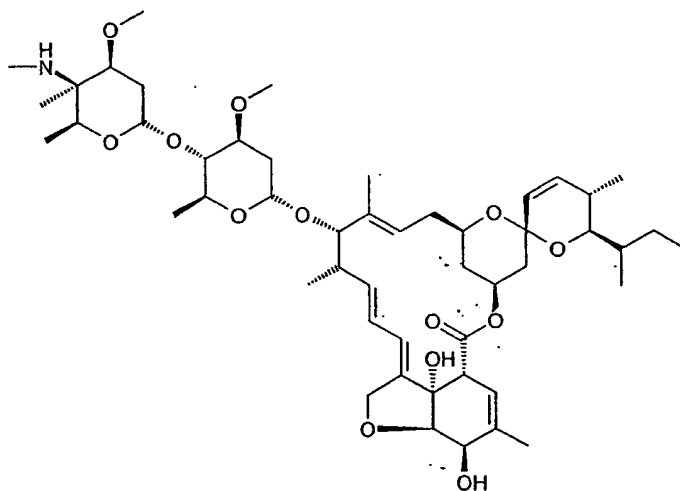
- Step A: 51.86 g 5-OTBDMS-4''-desoxy-4''-oxo-avermectin B<sub>1</sub> are dissolved in 200 ml methanol, 13.1 ml pyridine and 13.19 g N-methylhydroxylamine hydrochlorid are added.
- 5 The mixture is stirred at room temperature for 5 hours, poured into sodium hydrogencarbonate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 5-OTBDMS-4''-desoxy-4''- methyloxidoimino-Avermectin B<sub>1</sub>.
- 10 Step B: To a solution of 1g of 5-OTBDMS-4''-desoxy-4''-methyloxidoimino -Avermectin B<sub>1</sub> (obtained in step A) in 15 ml of tetrahydrofuran at 0°C is added 0.98 ml of methylmagnesium chloride (3M) and the mixture is stirred at 0°C for 30 minutes, then the ice bath is removed. 0.45 ml of methylmagnesium chloride (3M) is added to the solution at RT, and the mixture is stirred at room temperature for 10 minutes, poured into a saturated
- 15 sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 5-OTBDMS-4''-(R)- 4''-desoxy -4''-N-methyl hydroxylamino-4''-methyl -Avermectin B<sub>1</sub>.
- Step C: 0.300 g of 5-OTBDMS-4''-(R)- 4''-desoxy -4''-N-methyl hydroxylamino-4''-methyl -
- 20 Avermectin B<sub>1</sub> are dissolved in 7.5 ml tetrahydrofuran, then 3 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and

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extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(*R*)-4''-desoxy-4''-N-methyl hydroxylamino-4''-methyl -Avermectin B<sub>1</sub>.

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Example P4: 4''-(*R*)-4''-desoxy-4''-methyl-4''-N-methylamino-Avermectin B<sub>1</sub>



Step A : 10.85g of 5-OTBDMS-4''-(*R*)-4''-desoxy-4''-N-methyl hydroxylamino-4''-methyl -  
 10 Avermectin B<sub>1</sub> (P3: Steps A and B) are dissolved in 360 ml of a mixture of acetonitrile /  
 water (3 :1), then 8.08 g of molybdenumhexacarbonyl are added. The mixture is stirred at  
 room temperature for 6 hours, poured into sodium hydrogencarbonate, and extracted with  
 ethylacetate. Then the phases are separated; the organic phase is dried over sodium  
 sulfate and the solvents are distilled off. The residue is purified by chromatography on  
 15 silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4''-(*R*)-4''-desoxy-4''-N-  
 methylamine-4''-methyl -Avermectin B<sub>1</sub> and 5-OTBDMS-4''-(*R*)-4''-desoxy-4''-amino-4''-  
 methyl-Avermectin B<sub>1</sub>.

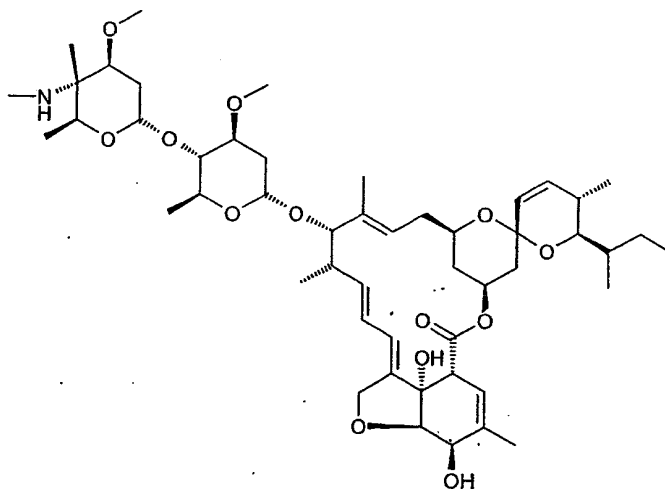
Step B: 0.210 g of 5-OTBDMS-4''-(*R*)-4''-desoxy-4''-N-methylamine-4''-methyl -Avermectin  
 B<sub>1</sub> are dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is  
 20 prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The  
 mixture is stirred at room temperature for 24 hours, poured into a solution of sodium

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hydrogencarbonate and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 4''-(R)-4''-desoxy-4''-N-methylamine-4''-methyl-Avermectin B<sub>1</sub>.

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Example P5: 4''-(S)-4''-desoxy-4''-N-Methylamino-4''-methyl-Avermectin B<sub>1</sub>



- Step A: To 11.09 g of 5-OTBDMS-4''-desoxy-4''-phenylsulfinimine-Avermectin B<sub>1</sub> (P1: Steps A and B) in 150 ml of tetrahydrofuran at 0°C is added 11 ml of methylmagnesium chloride (3M) and the mixture is stirred at 0°C for 30 minutes; then the ice bath is removed. Then 10 ml of methyl iodine is added to the solution at RT, and the mixture is stirred at room temperature for 24 hours, poured into a saturated sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo*.
- 15 The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4''-(S)-4''-desoxy-4''-(N-phenylsulfoxid-N-methyl)amino-4''-methyl-Avermectin B<sub>1</sub>.

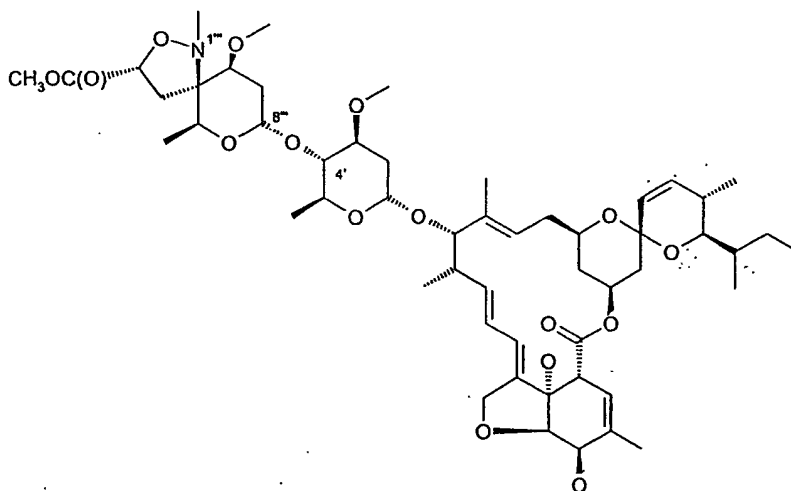
- Step B: 0.120 g of 5-OTBDMS-4''-(S)-4''-desoxy-4''-(N-phenylsulfoxid-N-methyl)amino-4''-methyl-Avermectin B<sub>1</sub> are dissolved in 3 ml tetrahydrofuran, then 0.6 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridin, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a solution of sodium hydrogencarbonate and extracted with ethylacetate. Then the phases are
- 20



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separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 4''-(S)-4''-desoxy-4''-N-methylamino-4''-methyl-Avermectin B<sub>1</sub>.

- 5 Example P6: 4'-O-[(3'''R,5'''R,6'''S,8'''S,10'''S)-10'''-methoxy-3'''-methoxycarbonyl-1'''',6'''-dimethyl-2'''',7'''-dioxo-1'''-aza-spiro[4.5]deca-8'''-yl]-avermectin B<sub>1</sub> monosaccharide



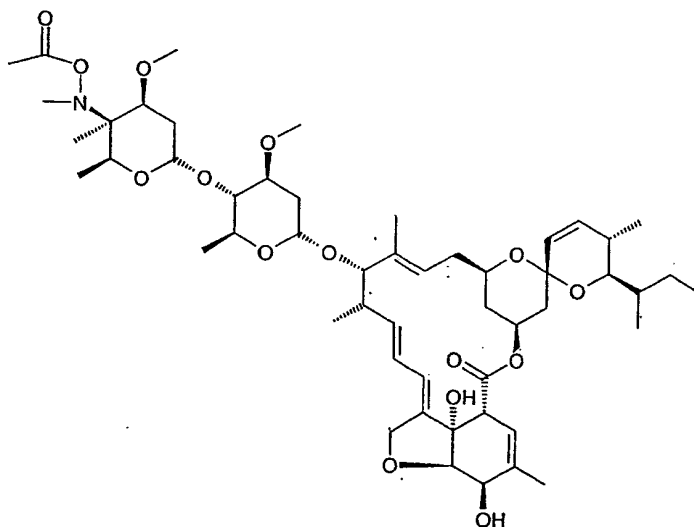
- Step A : 0.5 g of 5-OTBDMS-4''-desoxy-4''- methyl-oxidoimino-Avermectin B<sub>1</sub> (P3: Step A) are dissolved in 5 ml of toluene, 0.16 ml of acrylic acid methyl ester is added. The mixture is stirred at room temperature for 24 hours, poured on silica gel and eluted with hexane/ethylacetate (3 : 1) to yielding 5-OTBDMS-4''-(R)-4''-desoxy-4''-(2'''-Methyl-isoxazolidine-5'''-carboxylic acid methyl ester)-avermectin B<sub>1</sub>.

- Step B: 0.200 g of 5-OTBDMS-4''-(R)-4''-desoxy-4''-(2'''-methyl-isoxazolidine-5'''-carboxylic acid methyl ester)-avermectin B<sub>1</sub> are dissolved in 5 ml tetrahydrofuran, then 2 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a solution of sodium hydrogencarbonate and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane / ethylacetate,

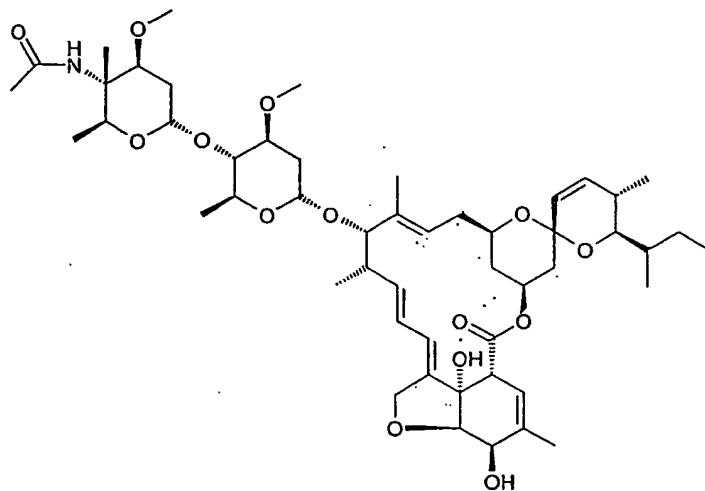
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yielding 4''-(R)-4''-desoxy-4''-(2'''-methyl-isoxazolidine-5'''-carboxylic acid methyl ester)-  
 avermectin B<sub>1</sub>.

Example P7: 4''-(R)- 4''-desoxy -4''-N-methyl-N-(methylcarbonyloxy-amino)-4''-methyl-  
 5 avermectin B<sub>1</sub>.



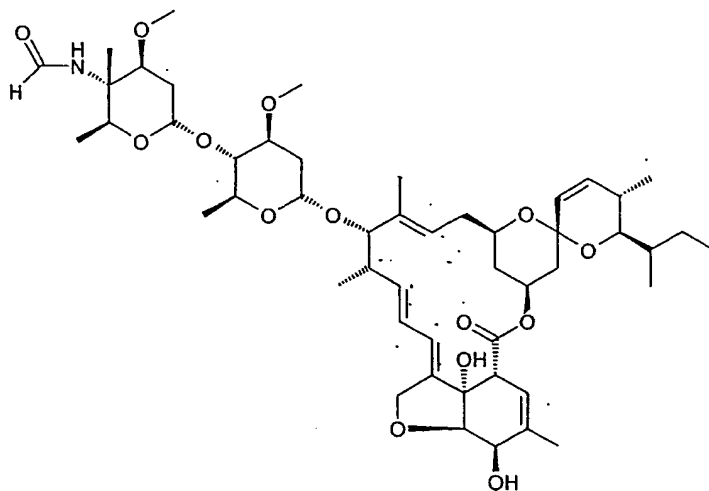
1080 mg 5-OTBDMS-4''-(R)- 4''-desoxy -4''-N-methyl-hydroxylamine-4''-methyl -avermectin  
 B<sub>1</sub> (P3: Steps A and B) are dissolved in 20 ml dichloromethane, 1250 mg  
 10 dimethylaminopyridine, 370  $\mu$ l acetylchloride are added. The mixture is stirred at room  
 temperature for 30 minutes. The reaction mixture is poured into saturated sodium  
 hydrogencarbonate, extracted with ethylacetate, dried over Mg<sub>2</sub>SO<sub>4</sub>, and concentrated *in*  
*vacuo*. 300 mg of the residue is dissolved in 7.5 ml tetrahydrofuran, then 1.5 ml of a stock  
 solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran  
 15 and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into  
 water, and extracted with ethylacetate. Then the phases are separated; the organic phase  
 is dried over sodium sulfate and the solvents are distilled off. The residue is purified by  
 chromatography on silica gel with hexane/ethylacetate, yielding 4''-(R)- 4''-desoxy -4''-N-  
 methyl-N-(methylcarbonyloxy-amino)-4''-methyl-avermectin B<sub>1</sub>.

Example P8: 4''-(S)- 4''-desoxy -4''-acetyl-amino-4''-methyl-Avermectin B<sub>1</sub>

Step A : To a solution of 0.2 g of 5-OTBDMS-4''-(S)- 4''-desoxy -4''-amino-4''-methyl-Avermectin B<sub>1</sub> (P1: Steps A to D) and 0.16 ml of pyridine in 4 ml tetrahydrofuran at room temperature is added 0.07 ml of acetyl chloride. The mixture is stirred for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The 5-OTBDMS-4''-(S)- 4''-desoxy -4''-acetyl-amino-4''-methyl-Avermectin B<sub>1</sub> is used without further purification.

Step B: 5-OTBDMS-4''-(S)- 4''-desoxy -4''-acetyl-amino-4''-methyl-Avermectin B<sub>1</sub> is dissolved in 6 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S)- 4''-desoxy -4''-acetyl-amino-4''-methyl-Avermectin B<sub>1</sub>.

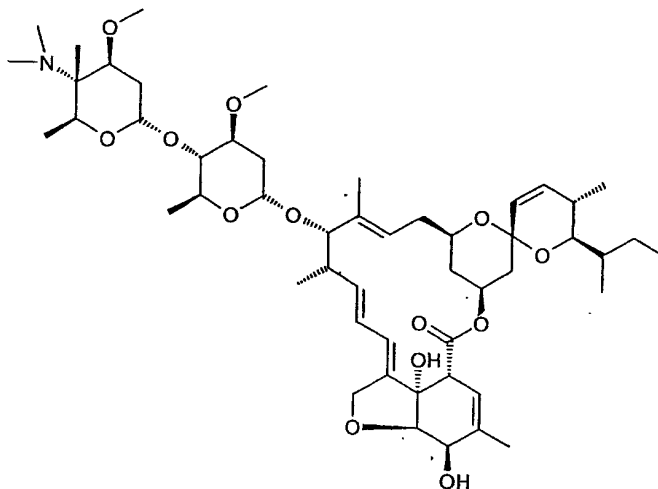
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Example P9: 4''-(S)- 4''-desoxy -4''-formylamino-4''-methyl-Avermectin B<sub>1</sub>

Step A : To a solution of 0.125 g of 5-OTBDMS-4''-(S)- 4''-desoxy -4''-amino-4''-methyl-Avermectin B<sub>1</sub> (P1: Steps A to D) in 6 ml ethylacetate and 12 ml of sodium hydrogencarbonate (1M) at room temperature is added 0.11 ml of acetic formic anhydride. The mixture is stirred for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The 5-OTBDMS-4''-(S)- 4''-desoxy -4''-formylamino-4''-methyl-Avermectin is used without further purification.

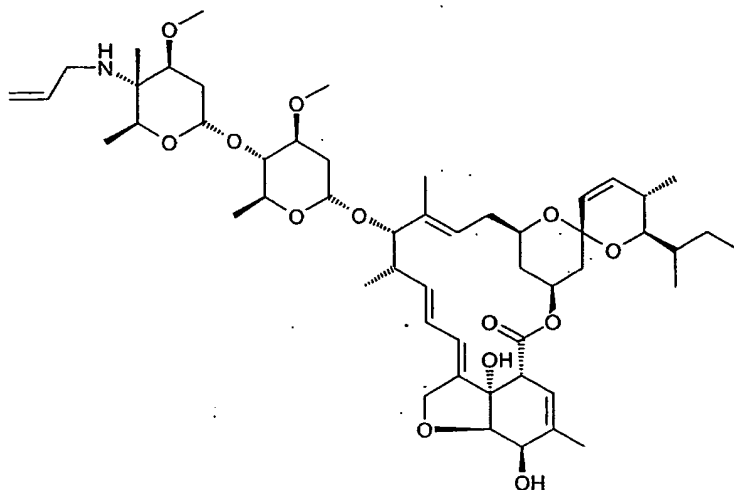
Step B: 5-OTBDMS-4''-(S)- 4''-desoxy -4''-formylamino-4''-methyl-Avermectin is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate, yielding 4''-(S)- 4''-desoxy -4''-formylamino-4''-methyl-Avermectin B<sub>1</sub>.

Example P10: 4''-(S)- 4''-desoxy -4''-N, N-dimethylamino-4''-methyl-Avermectin B<sub>1</sub>



Step A : To a solution of 0.2 g of 5-OTBDMS-4''-(S)- 4''-desoxy -4'' -amino-4''-methyl-Avermectin B<sub>1</sub> (P1: Steps A to D) and 0.162 mg of acid pivalic in acetonitrile at room temperature is added 0.08 ml of formaldehyde (37%). The mixture is stirred for 2 hours. Then 0.02 g of sodium cyanoborohydride is added. The mixture is stirred for 18 hours. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethylacetate, extracted with ethylacetate, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The 5-OTBDMS-4''-(S)- 4''-desoxy -4''-N, N-dimethylamino-4''-methyl-Avermectin B<sub>1</sub> is used without further purification.

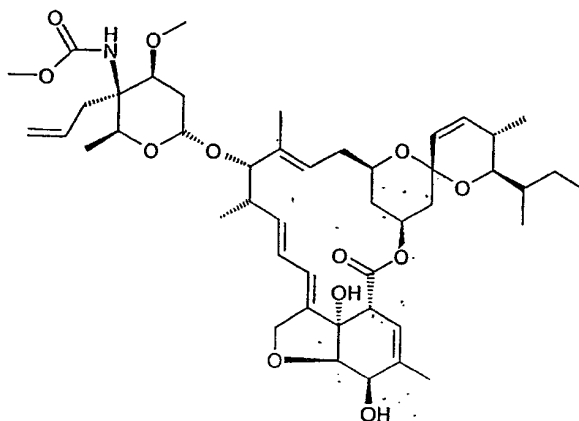
Step B: 5-OTBDMS-4''-(S)- 4''-desoxy -4''-N, N-dimethylamino-4''-methyl-Avermectin B<sub>1</sub> is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate, yielding 4''-(S)- 4''-desoxy -4''-N, N-dimethylamino-4''-methyl-Avermectin B<sub>1</sub>.

Example P11: 4''-(S)- 4''-desoxy -4''-N-allylamino-4''-methyl-Avermectin B<sub>1</sub>

Step A : To a solution of 0.165 g of 5-OTBDMS-4''-(S)- 4''-desoxy -4'' -amino-4''-methyl-Avermectin B<sub>1</sub> (P1: Steps A to D) and 0.138 mg of potassium carbonate in 8 ml acetonitrile is added 0.1 ml of allylbromide. The mixture is stirred for 3 hours at reflux. The mixture is poured into water and ethylacetate, extracted with ethylacetate, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue is used without further purification.

Step B: 5-OTBDMS-4''-(S)- 4''-desoxy -4''-N-allylamino-4''-methyl-Avermectin B<sub>1</sub> (obtained from Step A) is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S)- 4''-desoxy -4''-N-allylamino-4''-methyl-Avermectin B<sub>1</sub>.

Example P12: 4'-(*R*)- 4'-desoxy -4'-methyloxycarbonylamino-4'-allyl-Avermectin B<sub>1</sub> monosaccharide.

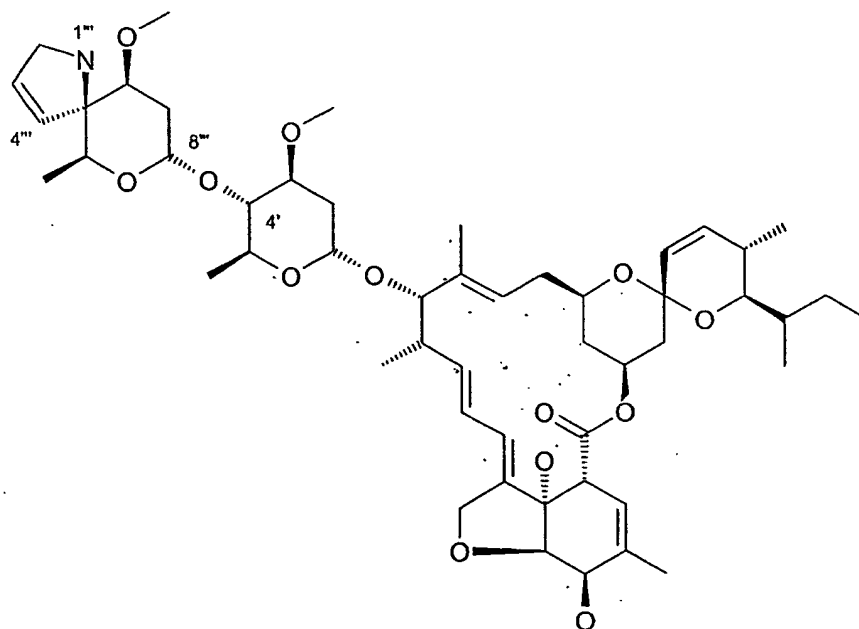


- 5 Step A : To a solution of 0.3 g of 5-OTBDMS-4'-(*R*)- 4'-desoxy -4'-amino-4'-allyl-Avermectin B<sub>1</sub> monosaccharide (obtained by the same reactions that with the disaccharide derivative - P1: Steps A, B, C (Grignard is allylmagnesium bromide) and D) 6 ml of sodium hydrogencarbonate (1M) and 10 ml of ethylacetate at room temperature is added 0.06 ml of methyl chloroformate. The mixture is stirred for 1 hour. The mixture is poured into a
- 10 saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue is used without further purification.

- Step B: 5-OTBDMS-4'-(*R*)- 4'-desoxy-4'-methyloxycarbonylamino-4'-allyl-Avermectin B<sub>1</sub> monosaccharide is dissolved in 8 ml tetrahydrofuran, then 1.6 ml of a stock solution are
- 15 added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with
- 20 ethylacetate, yielding 4'-(*R*)- 4'-desoxy-4'-methyloxycarbonylamino-4'-allyl-Avermectin B<sub>1</sub> monosaccharide.



**Example P13:** 4'-O-[(5'''R,6'''S,8'''S,10'''S)-10'''-Methoxy-6'''-methyl-7'''-oxa-1'''-aza-spiro[4.5]dec-3'''-en-8'''-yl]-avermectin B1 monosaccharide.



5 Step A : To a solution of 1 g of 5-OTBDMS-4''-(R)- 4''-desoxy- 4''-N-allylamino-4''-vinyl-  
Avermectin B<sub>1</sub> (P1: Steps A, B, C (Grignard is vinylmagnesium bromide) and D, and P11:  
Step A) in 50 ml of dichloromethane is added 0.07 ml of trifluoroacetic acid, 0.07 ml of  
tetraisopropyltitanium. The mixture is stirred for 1 hour at reflux. Then 0.1 g of Grubb's  
catalyst is added. The mixture is stirred for 24 hour at reflux, then 0.3 g of Grubb's catalyst  
10 and 0.14 ml of tetraisopropyltitanium are added. The mixture is stirred for 24 hour at reflux.  
The solvent is removed under vacuum and the residue is used without further purification.

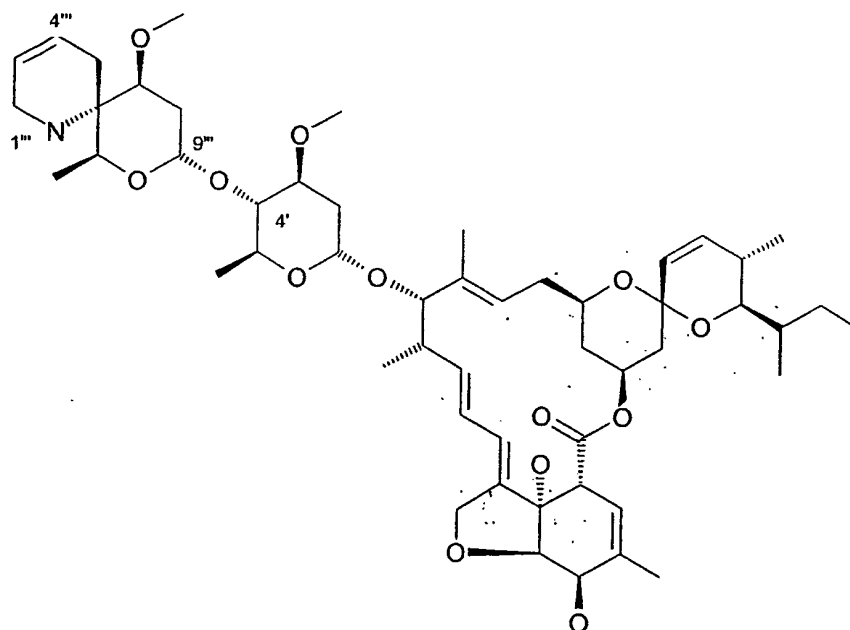
Step B: 5-OTBDMS-4''-(R)- 4''-desoxy- 4''- (4'',4'''-dihydro-1H-pyrrole) Avermectin B<sub>1</sub> (obtained from Step A) is dissolved in 25 ml tetrahydrofuran, then 10 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with

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hexane/tetrahydrofuran, yielding 4''-(R)- 4''-desoxy- 4''- (4'',4'''-dihydro-1H-pyrrole) Avermectin B<sub>1</sub>.

Example P14: 4'-O-[(6'''S,7'''S,9'''S,11'''S)-11'''-Methoxy-7'''-methyl-8'''-oxa-1'''-aza-

5 spiro[5.5]undec-3'''-en-9'''-yl]-avermectin B1 monosaccharide.



Step A : To a solution of 0.6 g of 5-OTBDMS-4''-(S)- 4''-desoxy- 4''-N-allylamino-4''-allyl-Avermectin B<sub>1</sub> (P1: Steps A, B, C (Grignard is allylmagnesium bromide) and D, and P11: Step A) in 30 ml of dichloromethane is added 0.05 ml of trifluoroacetic acid, 0.05 ml of tetraisopropyltitanium. The mixture is stirred for 1 hour at reflux. Then 0.06 g of Grubb's catalyst is added. The mixture is stirred for 24 hour at reflux, then 0.12 g of Grubb's catalyst and 0.10 ml of tetraisopropyltitanium are added. The mixture is stirred for 24 hour at reflux. The solvent is removed under vacuum and the residue is used without further purification.

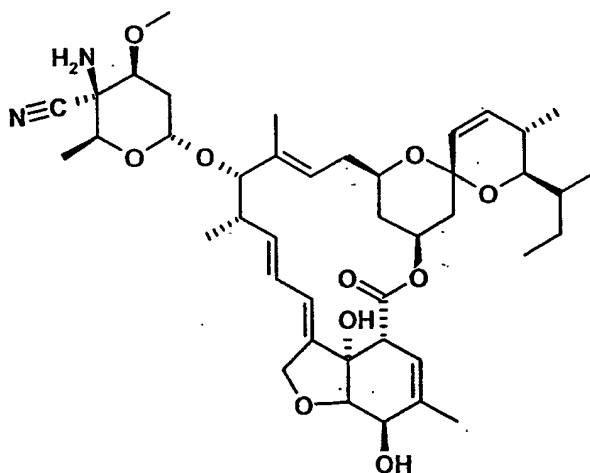
Step B: 5-OTBDMS-4''-(S)- 4''-desoxy- 4''- (1''', 4'', 3''', 6'''-tetrahydro-pyridine) Avermectin B<sub>1</sub> (obtained from Step A) is dissolved in 15 ml tetrahydrofuran, then 6 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with

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ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/tetrahydrofuran (1/2), yielding 4'-(S)- 4"-desoxy- 4"- (1''', 4'', 3''', 6'''-tetrahydro-pyridine) Avermectin B<sub>1</sub>.

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Example P15: 4'-(R)-4'-desoxy-4'-amino-4'-cyano-avermectin B1 monosaccharide

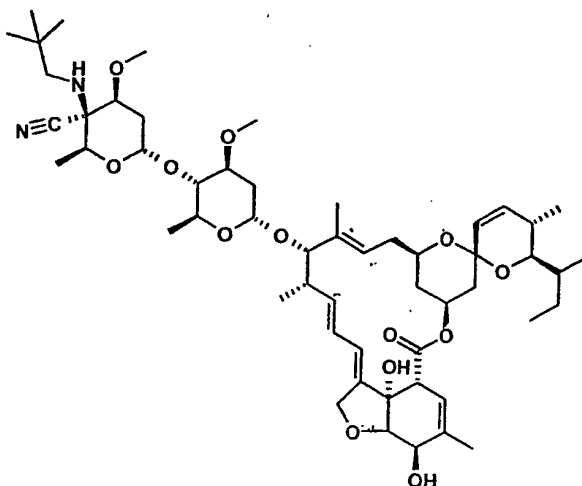


- 10 Step A: 3.0 g 4'-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 monosaccharide are dissolved in 20 ml ethyl acetate, then 2.14 ml hexamethyldisilazane and 450 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 600 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase
- 15 dried with sodium sulfate and the solvent evaporated.

- Step B: The crude product from Step A is dissolved in 20 ml methanol, the solution cooled to 0 °C, and 0.21 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 30 minutes, then 20 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted
- 20 with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4'-(R)-4'-desoxy-4'-amino-4'-cyano-avermectin B1 monosaccharide.

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Example P16: 4''-(R)-4''-desoxy-4''-(2,2-dimethyl-propylamino)-4''-cyano-avermectin B1

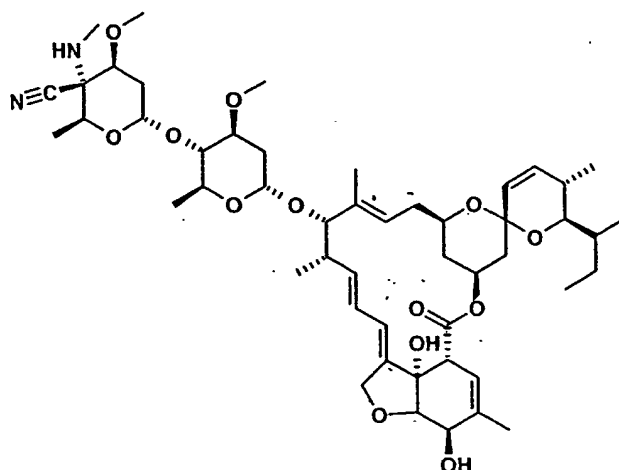


- 5 Step A: 4.0 g 4''-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 30 ml toluene, then 2.1 g 2,2-dimethyl-propylamine, 1.0 g zinc chloride and 0.93 ml trimethylsilyl chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 1.9 ml trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.
- 10

- Step B: The crude product from Step A is dissolved in 40 ml methanol, the solution cooled to 0 °C, and 0.36 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 30 minutes, then 40 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4''-(R)-4''-desoxy-4''-(2,2-dimethyl-propylamino)-4''-cyano-avermectin B1.
- 15

Example P17: 4''-(S)-4''-desoxy-4''-methylamino-4''-cyano-avermectin B1

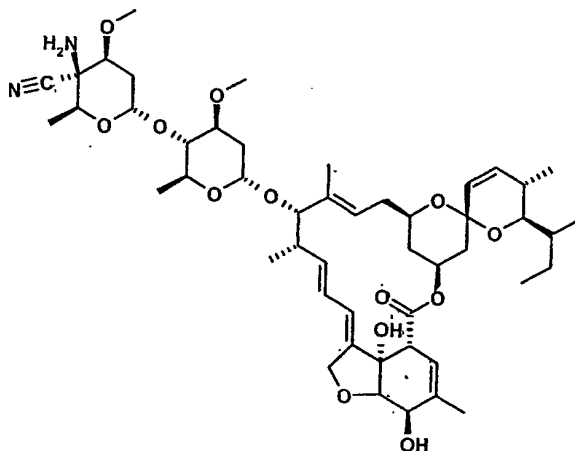
-111-



- Step A: 2.0 g 4''-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 10 ml ethyl acetate, then 1.5 ml heptamethyldisilazane and 300 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 600 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.
- 10 Step B: The crude product from Step A is dissolved in 10 ml methanol, the solution cooled to 0 °C, and 0.08 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 45 minutes, then 10 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl
- 15 acetate, yielding 4''-(S)-4''-desoxy-4''-methylamino-4''-cyano-avermectin B1.

Example P18: 4''-(R)-4''-desoxy-4''-amino-4''-cyano-avermectin B1

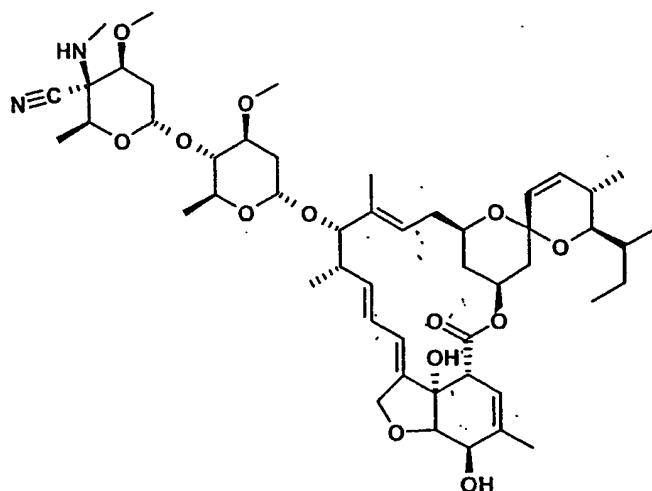
-112-



- Step A: 2.0 g 4''-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 10 ml ethyl acetate, then 1.4 ml hexamethyldisilazane and 300 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 400 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.
- 10 Step B: The crude product from Step A is dissolved in 20 ml methanol, the solution cooled to 0 °C, and 0.12 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 45 minutes, then 20 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4''-(R)-4''-desoxy-4''-amino-4''-cyano-avermectin B1.
- 15

Example P19: 4''-(R)-4''-desoxy-4''-methylamino-4''-cyano-avermectin B1

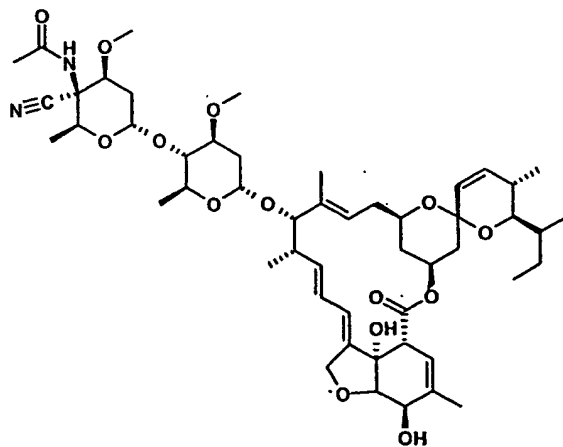
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2.0 g 4''-(R)-4''-desoxy-4''-amino-4''-cyano-avermectin B1 (P18) are dissolved in 20 ml ethyl acetate, then 16 ml methyl iodide and 20 ml aqueous 1N sodium bicarbonate are added.

- 5 The mixture is stirred vigorously at 60 °C for 18 hours. Then the reaction mixture is cooled to room temperature, the phases separated, the organic phase dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4''-(R)-4''-desoxy-4''-methylamino-4''-cyano-avermectin B1.

- 10 Example P20: 4''-(R)-4''-desoxy-4''-acetyl-amino-4''-cyano-avermectin B1



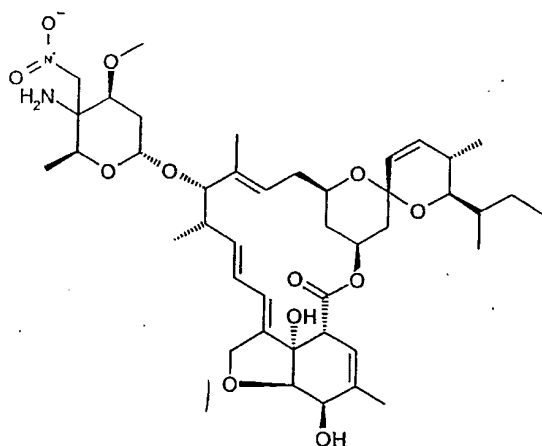
- 15 3.0 g 4''-(R)-4''-desoxy-4''-amino-4''-cyano-avermectin B1 (P18) are dissolved in 20 ml ethyl acetate, then 20 ml aqueous 1N sodium bicarbonate are added. The mixture is stirred

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vigorously and 1.6 ml acetylchloride are added. Stirring is continued at room temperature for 4 hours. Then the phases are separated, the organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4'-(R)-4'-desoxy-4'-acetylamino-4"-cyano-avermectin B1.

5

Example P21: 4'-(R)-4'-desoxy-4'-amino-4'-nitromethyl-avermectin B1 monosaccharide and 4'-(S)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide.



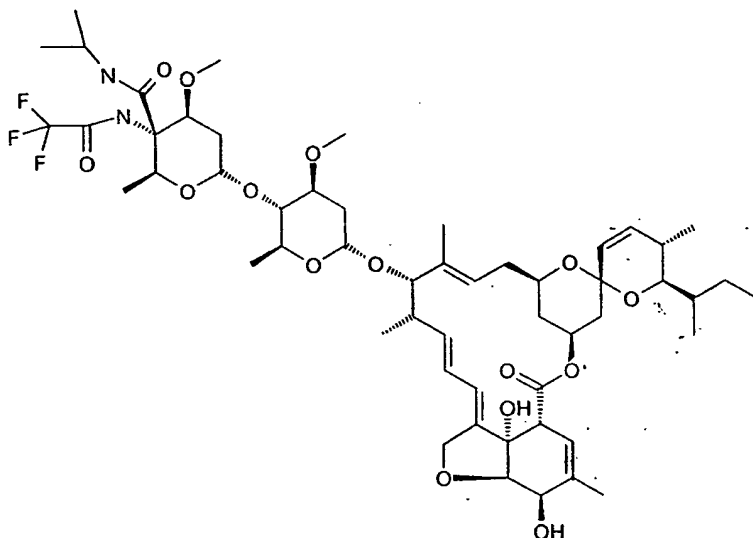
- 10 Step A: To a solution of 13g of 5-OTBDMS-4'-desoxy-4'-phenylsulfinimine-Avermectin B<sub>1</sub> (obtained by the method described in step A and B : Exemple P1) in 110 ml of nitromethane at RT is added 5900 µl of piperidine. The mixture is stirred at room temperature for 1 hour. Then, the solvents are distilled off. The residue is dissolved in methanol at 0°C then 5 eq. of methanesulfonic acid were added. The mixture is stirred at 0
- 15 °C for 30 minutes, then saturated solution of sodium bicarbonate is added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with cyclohexane/ethyl acetate, yielding 4'-(R)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide and 4'-(S)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide.

20



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Example P22: 4''-(S)-4''-desoxy-4''-trifluoroacetyl-amino-4''- isopropylcarbamoyl-avermectin B<sub>1</sub>



5 Step A: To a solution of 7.39g of 5-OTBDMS-4''-desoxy-4''-phenylsulfinimine-Avermectin B<sub>1</sub> (obtained in step A, B : Exemple P1) in 150 ml of dichloromethane at -78°C is added 1970 µl of Pyridine, 840 µl of isopropylisocyanide and 940 µl of trifluoroacetic acid. The mixture is stirred overnight at room temperature. The mixture is poured into a saturated sodium hydrogenocarbonate and ethylacetate, extracted with ethylacetate; the organic phase is

10 dried over sodium sulfate, and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with cyclohexane/ethyl acetate, yielding 5-O-*t*-butyldimethylsilyl-4''-(S)-4''-desoxy-4''-trifluoroacetyl-amino-4''- isopropylcarbamoyl-avermectin B<sub>1</sub>.

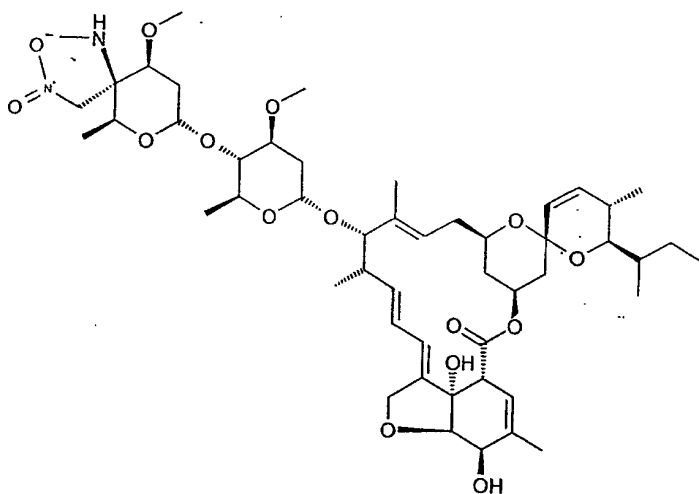
Step B: 5-O-*t*-butyldimethylsilyl-4''-(S)-4''-desoxy-4''-trifluoroacetyl-amino-4''- isopropylcarbamoyl-avermectin B<sub>1</sub>. (obtained from Step A) is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution is added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogenocarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over

20 sodium sulfate and the solvents are distilled off. The residue is purified by chromatography

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on silica gel with hexane/ethylacetate, yielding : 4''-(S)-4''-desoxy-4''-trifluoroacetyl-amino-4''-isopropylcarbamoyl-avermectin B1.

5 Example P23: 4''-(R)-4''-desoxy-4''-amino-N-methyl-4''-nitromethyl-avermectin B1.



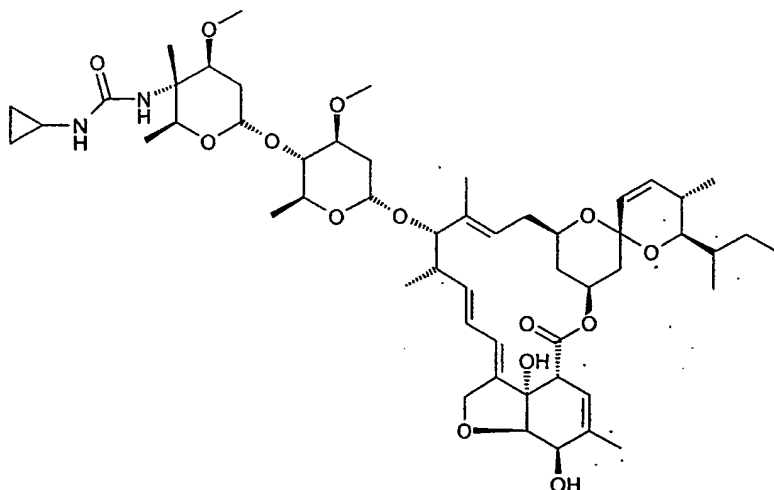
10 Step A: 3 g 4''-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 20 ml ethyl acetate, then 1.82g heptamethyldisilazane and 430 mg zinc chloride are added. The mixture is stirred at 70 °C for 3 hours. Then the solvents are distilled off. The crude residue is dissolved in 10 ml of nitromethane and 440 µl of piperidine is added. The mixture is stirred at room temperature overnight. The solvents are distilled off and the residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 5-O-*t*-butyldimethylsilyl-7-trimethylsilyl-4''-(R)-4''-desoxy-4''-amino-N-methyl-4''-methylnitro-  
15 avermectin B1.

Step B: 5-O-*t*-butyldimethylsilyl-7-trimethylsilyl-4''-(R)-4''-desoxy-4''-amino-N-methyl-4''-methylnitro-avermectin B1. (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 01g), then a stock solution is added (0.5 mL by 01g of starting material), which is

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prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 4''-(R)-4''-desoxy-4''-amino-N-methyl-4''-methylnitro-  
 5 avermectin B<sub>1</sub>.

Example P24: 4''-(S)-4''-desoxy-4''-(cyclopropylaminocarbonyl-amino)-4''-methyl-  
 10 Avermectin B<sub>1</sub>



Step A : To a solution of 1 g of 5-OTBDMS-4''-(S)-4''-desoxy-4''-amino-4''-methyl-  
 15 Avermectin B<sub>1</sub> (P1: Steps A to D) and 1.4 ml of triethylamine in 20 ml dichloromethane at room temperature is added 1g of p-nitrophenyl chloroformate. The mixture is stirred for 45 minutes. The mixture is poured into a saturated solution of sodium hydrogencarbonate and dichloromethane, washed with water (2x), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The 5-OTBDMS-4''-(S)-4''-desoxy-4''- carbamic acid p-nitrophenyl ester-4''-methyl-  
 20 Avermectin B<sub>1</sub> is used without further purification.

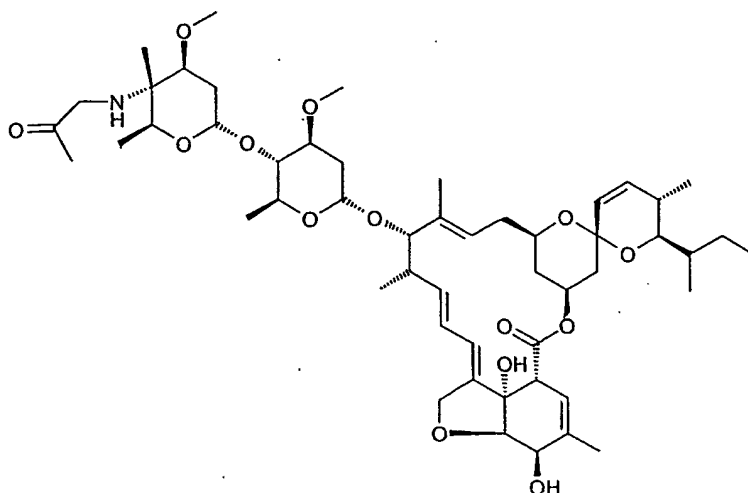
Step B: 5-OTBDMS-4''-(S)- 4''-desoxy -4''- carbamic acid p-nitrophenyl ester-4''-methyl-Avermectin B<sub>1</sub>. (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from  
5 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding  
10 4''-(S)- 4''-desoxy -4''- carbamic acid p-nitrophenyl ester-4''-methyl-Avermectin B<sub>1</sub>.

Step C : To a solution of 1 g of 4''-(S)- 4''-desoxy -4''- carbamic acid p-nitrophenyl ester-4''-methyl-Avermectin B<sub>1</sub>. (Step B) and 0.18 ml of triethylamine in 10 ml dichloromethane at room temperature is added 45 µl of cyclopropylamine. The mixture is stirred for 30 minutes.  
15 The mixture is concentrated *in vacuo* and the residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S) -4''-desoxy-4''-cyclopropyl-urea-4''-methyl-Avermectin B<sub>1</sub>.

Using the same reaction, it is possible to reverse the order of step B and C.

20 Example P25: 4''-(S) -4''-desoxy-4''- (propan-2-on-1-yl-amino)-4''-methyl-Avermectin B<sub>1</sub>

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Step A : To a solution of 0.420 mg g of 5-OTBDMS-4''-(S)-4''-desoxy-4''- amino-4''-methyl-Avermectin B<sub>1</sub> in 5 ml of ethylacetate at room temperature and 5 ml of sodium hydrogencarbonate (1M) is added 380 µl of methylbromoacetate. The mixture is stirred overnight. The aqueous phase and the organic phase are separated. The organic phase mixture is washed with water and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4''-(S)-4''-desoxy-4''- amino propan-2-one-4''-methyl-Avermectin B<sub>1</sub>.

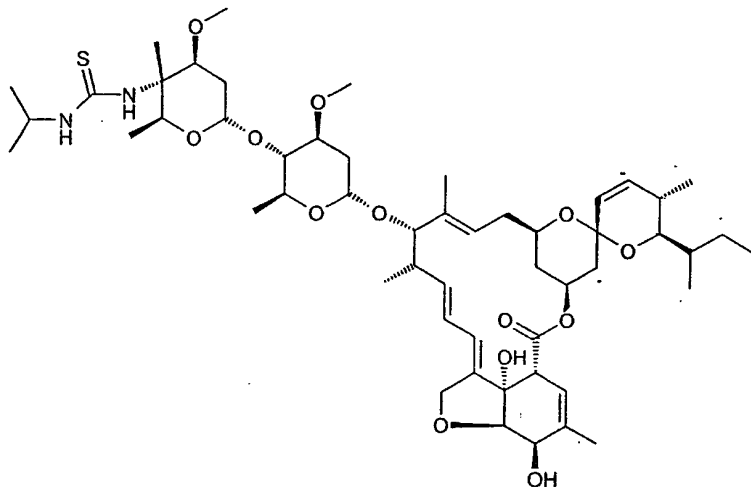
10

Step B: 5-OTBDMS-4''-(S)-4''-desoxy-4''- amino propan-2-one-4''-methyl-Avermectin B<sub>1</sub> (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S)-4''-desoxy-4''- amino propan-2-one-4''-methyl-Avermectin B<sub>1</sub>.

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Example P26: 4''-(S) -4''-desoxy-4''-(isopropylaminothiocarbonyl-amino)-4''-methyl-Avermectin B<sub>1</sub>



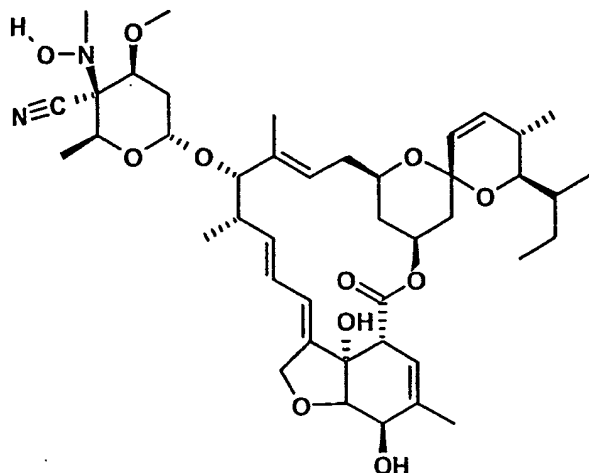
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Step A : To a solution of 0.2 g of 5-OTBDMS-4''-(S) -4''-desoxy-4''- amino -4''-methyl-Avermectin B<sub>1</sub> in 3 ml tetrahydrofuran at room temperature is added 220 mg of isopropyl isothiocyanate. The mixture is stirred overnight at room temperature. The mixture is concentrated *in vacuo* and the residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4''-(S) -4''-desoxy-4''-isopropyl-thiourea-4''-methyl-Avermectin B<sub>1</sub>.

Step B: 5-OTBDMS-4''-(S) -4''-desoxy-4''-isopropyl-thiourea-4''-methyl-Avermectin B<sub>1</sub> (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S) -4''-desoxy-4''-isopropyl-thiourea-4''-methyl-Avermectin B<sub>1</sub>.

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Example P27 : 4'-(R)-4'-desoxy-4'- N-methyl-N-hydroxy-amino-4'-cyano-avermectin B1 monosaccharide

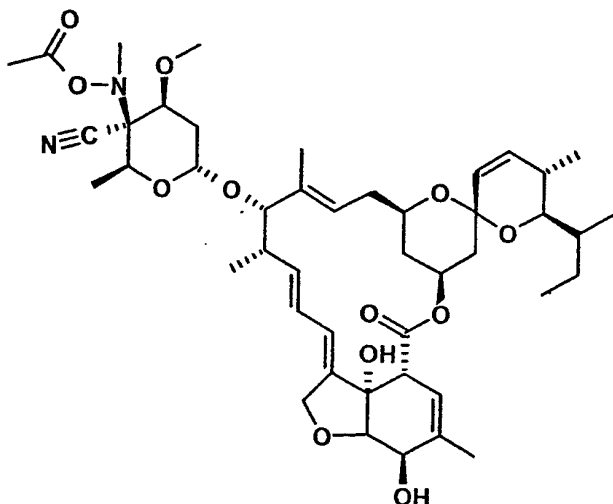


Step A: To a solution of 3020 mg of 5-OTBDMS-4'-desoxy-4'-methyloxidoimino -  
 5 Avermectin B<sub>1</sub> (obtained from avermectin B1 monosaccharide by analogy with Example P3, step A) in 80 ml of dichloromethane at RT is added 2190 µl of trimethylsilylcyanide. The mixture is stirred at room temperature for 4 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is washed with water and dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide.

Step B: 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off.  
 20 The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide.

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Example P28: 4'-(R)-4'-desoxy-4'- N-methyl-N-(methylcarbonyloxy-amino)-4'-cyano-  
 avermectin B1 monosaccharide.



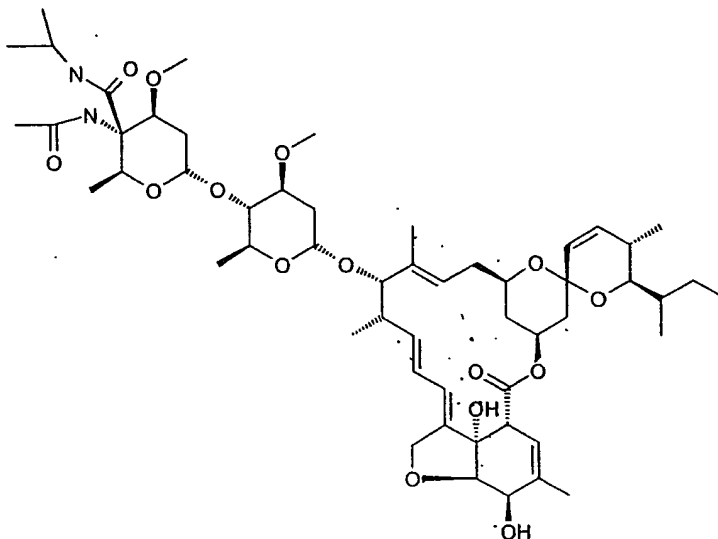
5

300 mg 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1  
 monosaccharide (P27: Steps A) are dissolved in 6 ml dichloromethane, and 410 mg  
 dimethylaminopyridine and 125  $\mu$ l acetylchloride are added. The mixture is stirred at room  
 temperature for 1 hour. The reaction mixture is filtered into silica gel with ethyl acetate and  
 concentrated under vacuum. The residue is dissolved in tetrahydrofuran (2.5 mL by 0.1g),  
 then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from  
 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred  
 at room temperature for 24 hours, poured into a mixture of saturated sodium  
 hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are  
 separated; the organic phase is dried over sodium sulfate and the solvents are distilled off.  
 The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding  
 4'-(R)-4'-desoxy-4'- N-methyl-N-(methylcarbonyloxy-amino)-4'-cyano-avermectin B1  
 monosaccharide.

20 Example P29: 4''-(S)-4''-desoxy-4''-acetyl-amino-4''- isopropylcarbamoxy-avermectin B1.



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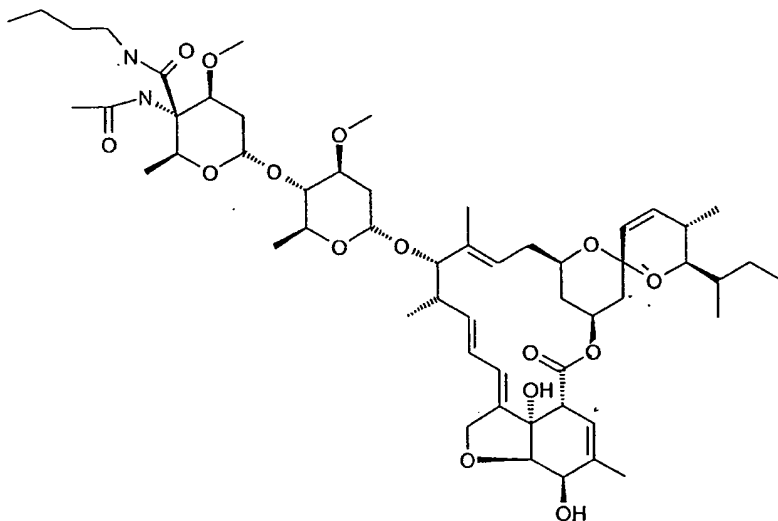
Step A: 2 g 5-OTBDMS-4''-desoxy-4''-oxo-avermectin B1 are dissolved in 4 ml methanol and the mixture is stirred at room temperature for 30 minutes. Then 0.15 g of ammoniumacetate and 0.19 ml of isopropylisocyanide are added. The mixture is stirred at room temperature for 20 hours. The mixture is poured into ethyl acetate and washed two times with a saturated solution of sodium hydrogencarbonate. Then the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding a mixture of 5-OTBDMS-4''-(S)-4''-desoxy-4''-acetylamino-4''- isopropylcarbamoyl-avermectin B1. and 5-OTBDMS-4''-(S)-4''-O-acetyl-4''- isopropylcarbamoyl-avermectin B1.

Step B: 1.1 g of the mixture (obtained from Step A) is dissolved in 35 ml of tetrahydrofuran, then 2.1 mL of a stock solution are added (which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine) and 6.1 mL of pyridine. The mixture is stirred at room temperature for 20 hours, poured into an aqueous solution of 5% of sodium hydrogencarbonate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4''-(S)-4''-desoxy-4''-acetylamino-4''- isopropylcarbamoyl-avermectin B1.

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Example P30: 4''-(S)-4''-desoxy-4''-acetylamino-4''- butylcarbamoyl-avermectin B1.



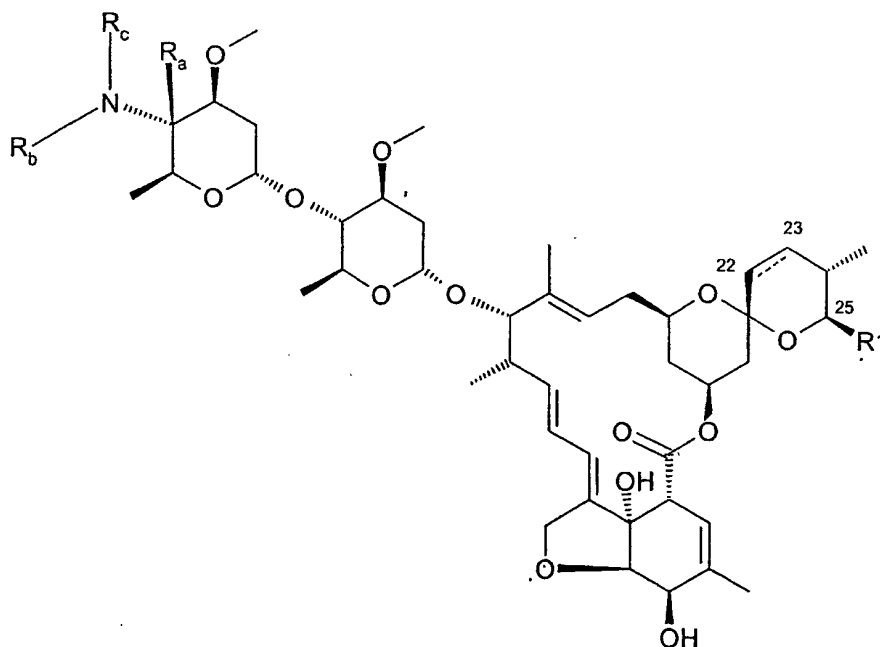
- 5 Step A: 2.03 g 5-OTBDMS-4''-(S)-4''-desoxy-4''-trifluoroacetylamino-4''- butylcarbamoyl-avermectin B1 are dissolved in 50 ml ethanol and 500 mg of sodium borohydride are added. The mixture is stirred at room temperature for 3 hours. Then 6 ml of a solution of sodium hydrogenocarbonate is added. The mixture is filtered and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate/methanol, yielding 5-OTBDMS-4''-(S)-4''-desoxy-4''-amino-4''- butylcarbamoyl-avermectin B1 (not pur,  
10 80% of purity).

- Step B: 0.2 g 5-OTBDMS-4''-(S)-4''-desoxy-4''-amino-4''- butylcarbamoyl-avermectin B1 are dissolved in 5.0 ml tetrahydrofuran. 120  $\mu$ l of pyridine and 50  $\mu$ l of acetylchloride are added.  
15 The mixture is stirred at room temperature for 30 minutes. The mixture is poured into ethyl acetate and washed two times with a saturated solution of sodium hydrogencarbonate. Then the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 5-OTBDMS -4''-(S)-4''-desoxy-4''-acetylamino-4''- butylcarbamoyl-avermectin B1.

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- Step C: 5-OTBDMS 4''-(S)-4''-desoxy-4''-acetylamino-4''- butylcarbamoyl-avermectin B1 (obtained from Step B) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 4''-(S)-4''-desoxy-4''-acetylamino-4''- butylcarbamoyl-avermectin B1.
- 10 The compounds of Tables 1-96, A-L and M1-M8 can be prepared in the same way as described in Examples P1 to P30, or by methods known to a person skilled in the art.

Table A: A compound of the formula



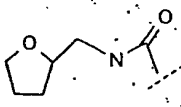
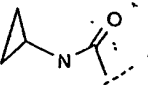
- wherein R<sub>1</sub> is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and
- 15

	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)

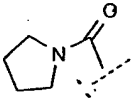
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					B1a	B1b
Table A1	W	CH <sub>3</sub>	H	H	5.71	5.39
Table A2	W	vinyl	H	H	6.03	5.55
Table A3	W	Allyl	H	H	6.13	5.87
Table A4	W	PhCH <sub>2</sub>	H	H	6.24	-
Table A5	Z	CH <sub>3</sub>	CH <sub>3</sub> C(O)	H	10.08	9.23
Table A6	W	vinyl	CH <sub>3</sub> C(O)	H	10.69	9.82
Table A7	W	Allyl	CH <sub>3</sub> C(O)	H	11.80	11.00
Table A8	W	CH <sub>3</sub>	HC(O)	H	10.08	-
Table A9	W	vinyl	HC(O)	H	10.67	9.76
Table A10	W	Allyl	HC(O)	H	11.65	-
Table A11	W	CH <sub>3</sub>	CH <sub>3</sub> OC(O)	H	11.22	10.44
Table A12	W	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H	11.31	10.67
Table A13	W	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	11.04	-
Table A14	W	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> C(O)	H	5.97	5.60
Table A15	W	CH <sub>3</sub>	ClCH <sub>2</sub> C(O)	H	10.41	9.60
Table A16	W	CH <sub>3</sub>	CH <sub>3</sub> C(O)OCH <sub>2</sub> C(O)	H	9.70	8.91
Table A17	W	CH <sub>3</sub>	CH <sub>3</sub> SCH <sub>2</sub> C(O)	H	10.54	9.87
Table A18	W	CH <sub>3</sub>	NCCH <sub>2</sub> C(O)	H	9.39	8.70
Table A19	Z	CH <sub>3</sub>	2-PySCH <sub>2</sub> C(O)	CH <sub>3</sub>	12.94	12.51
Table A20	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> C(O)	H	11.45	10.69
Table A21	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OCH <sub>2</sub> C(O)	H	12.57	12.02
Table A22	W	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	5.92	5.60
Table A23	W	PhCH <sub>2</sub>	CH <sub>3</sub>	CH <sub>3</sub>	7.25	6.88
Table A24	X	CH <sub>3</sub>	H <sub>2</sub> NSO <sub>2</sub>	H	10.85	-
Table A25	W	vinyl	allyl	H	10.40	10.14
Table A26	W	allyl	allyl	H	7.20	6.72
Table A27	W	Allyl	Propargyl	H	6.85	6.58
Table A28	W	CH <sub>3</sub>	allyl	H	4.17	3.91

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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A29	Z	CH <sub>3</sub>	CH <sub>3</sub>	H	4.99	-
Table A30	W	CN	iPrC(O)	CH <sub>3</sub>	10.53	-
Table A31	W	CN	CH <sub>3</sub> OC(O)	CH <sub>3</sub>	11.84	11.20
Table A32	W	CN	EtC(O)	CH <sub>3</sub>	9.87	9.20
Table A33	W	CN	EtOC(O)	CH <sub>3</sub>	11.18	10.54
Table A34	W	CN	(CH <sub>2</sub> CH <sub>2</sub> )CHC(O)	CH <sub>3</sub>	10.24	9.59
Table A35	W	CN	CH <sub>3</sub> CHCHC(O)	CH <sub>3</sub>	11.90	-
Table A36	W	CN	HC(O)	CH <sub>3</sub>	9.14	8.48
Table A37	W	CN	CH <sub>3</sub> C(O)	CH <sub>3</sub>	9.50	8.85
Table A38	W	CN	CH <sub>3</sub> OCH <sub>2</sub> C(O)	CH <sub>3</sub>	9.31	8.59
Table A39	W	CN	(CH <sub>3</sub> ) <sub>2</sub> CCHC(O)	CH <sub>3</sub>	10.48	9.84
Table A40	W	CN	CH <sub>3</sub>	CH <sub>3</sub>	12.04	11.42
Table A41	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CO	H	12.78	12.25
Table A42	Z	CH <sub>3</sub>	C(O)SCH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub>	H	13.35	12.98
Table A43	Z	CH <sub>3</sub>	C(O)SCH(CH <sub>3</sub> ) <sub>2</sub>	H	13.72	13.40
Table A44	Z	CH <sub>3</sub>	C(O)SEt	H	13.45	13.13
Table A45	Z	CH <sub>3</sub>		H	12.06	11.26
Table A46	Z	CH <sub>3</sub>	EtONHC(O)	H	12.43	11.79
Table A47	Z	CH <sub>3</sub>	CH <sub>3</sub> ONHC(O)	H	11.75	11.0
Table A48	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> NHC(O)	H	11.48	10.73
Table A49	Z	CH <sub>3</sub>		H	12.23	11.48
Table A50	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> NHC(O)	H	12.80	12.26

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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A51	Z	CH <sub>3</sub>		H	12.40	11.74
Table A52	Z	CH <sub>3</sub>	HCCCH <sub>2</sub> NHC(O)	H	12.22	11.53
Table A53	Z	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> NC(O)	H	11.80	11.01
Table A54	Z	CH <sub>3</sub>	CH <sub>3</sub> NHC(O)	H	11.22	10.40
Table A55	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> NC(O)	H	12.11	11.38
Table A56	Z	CH <sub>3</sub>	iPrNHC(S)	H	13.50	13.15
Table A57	Z	CH <sub>3</sub>	FCH <sub>2</sub> C(O)	H	12.08	11.37
Table A58	Z	CH <sub>3</sub>	F <sub>2</sub> CHC(O)	H	12.73	12.22
Table A59	W	CN	CH <sub>3</sub>	H	9.27	8.59
Table A60	Z	CH <sub>3</sub>	CH <sub>3</sub> CO	CH <sub>3</sub>	12.25	12.72
Table A61	Z	CH <sub>3</sub>	CH <sub>3</sub> NHC(S)	H	12.6	12.02
Table A62	Z	CH <sub>3</sub>	H <sub>2</sub> NC(O)CH <sub>2</sub>	H	5.00	4.58
Table A63	Z	CH <sub>3</sub>	CH <sub>3</sub> OC(O)CH <sub>2</sub>	H	6.19	5.68
Table A64	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)CH <sub>2</sub>	H	6.63	6.10
Table A65	Z	CH <sub>3</sub>	iPrOC(O)CH <sub>2</sub>	H	7.13	6.61
Table A66	Z	CH <sub>3</sub>	tBuOC(O)CH <sub>2</sub>	H	7.44	6.95
Table A67	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	CH <sub>3</sub>	14.91	-
Table A68	Z	CH <sub>3</sub>	Me <sub>2</sub> NOC(O)	H	12.85	12.35
Table A69	Z	CH <sub>3</sub>	CH <sub>3</sub> NHSO <sub>2</sub>	H	12.02	11.30
Table A70	Z	CH <sub>3</sub>	CH <sub>3</sub> SO <sub>2</sub>	H	12.17	11.46
Table A71	Y	CH <sub>3</sub>	tBuSO	H	9.34	8.76
Table A72	Z	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CClS(O)	H	13.33, 13.21	12.91, 12.77
Table A73	Z	HCC	H	H	5.04	4.59
Table A74	Z	HCC	CH <sub>3</sub> C(O)	H	10.92	10.16

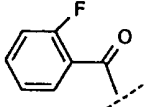
	LC MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A75	Z	HCC	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	11.89	11.16
Table A76	Z	HCC	CH <sub>3</sub> OC(O)	H	12.10	11.41
Table A77	Z	PhCH <sub>2</sub> NC(O)	CF <sub>3</sub> C(O)	H	14.10	-
Table A78	Z	CH <sub>3</sub>	H <sub>2</sub> NC(O)	H	10.30	9.48
Table A79	Z	IPrNHC(O)	CF <sub>3</sub> C(O)	H	13.98	13.72
Table A80	Z	tBuNHC(O)	CF <sub>3</sub> C(O)	H	15.60	15.36
Table A81	Z	BuNHC(O)	CF <sub>3</sub> C(O)	H	15.32	15.08
Table A82	Z	CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> NHC(O)	CF <sub>3</sub> C(O)	H	14.63	-
Table A83	Z	EtOC(O)CH <sub>2</sub> NHC(O)	CF <sub>3</sub> C(O)	H	14.61	14.34
Table A84	Z	C <sub>6</sub> H <sub>11</sub> NHC(O)	CF <sub>3</sub> C(O)	H	15.74	15.51
Table A85	Y	Me <sub>3</sub> SiCH <sub>2</sub> NHC(O)	CF <sub>3</sub> C(O)	H	6.64	6.07
Table A86	Z	CH <sub>3</sub> CC	H	H	11.12	10.48
Table A87	Y	CH <sub>3</sub> OCH <sub>2</sub> CC	H	H	7.37	7.02
Table A88	Y	CH <sub>3</sub>	-(CH <sub>2</sub> ) <sub>4</sub> -		3.67	3.47
Table A89	Y	CH <sub>3</sub> OCH <sub>2</sub> CC	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	8.51	7.90
Table A90	Y	CH <sub>3</sub>	BrCH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> OC(O)	H	10.68	10.8
Table A91	Y	CH <sub>3</sub> CC	CH <sub>3</sub> C(O)	H	7.98	7.34
Table A92	Y	CH <sub>3</sub> CC	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	8.80	8.21
Table A93	Y	CH <sub>3</sub> OCH <sub>2</sub> CC	CH <sub>3</sub> C(O)	H	7.82	7.19
Table A94	Y	BiCH <sub>2</sub> NHC(O)	CF <sub>3</sub> C(O)	H	10.40	10.18
Table A95	Y	tBuOC(O)N(CH <sub>2</sub> ) <sub>2</sub> NH C(O)	CF <sub>3</sub> C(O)	H	10.77	-
Table A96	Y	CH <sub>3</sub> NHC(O)	CF <sub>3</sub> C(O)	H	9.88	9.41
Table A97	Y	(CH <sub>2</sub> ) <sub>2</sub> CHNHC(O)	CF <sub>3</sub> C(O)	H	10.52	10.11
Table A98	Y	(CH <sub>2</sub> ) <sub>4</sub> CHNHC(O)	CF <sub>3</sub> C(O)	H	11.68	11.31
Table A99	Y	EtNHC(O)	CF <sub>3</sub> C(O)	H	10.48	-



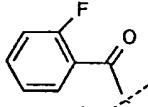
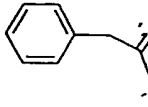
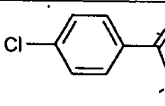
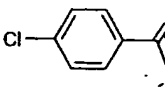
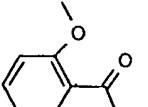
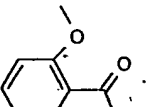
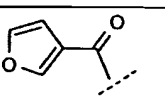
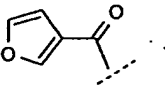
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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A100	Y	(CH <sub>2</sub> ) <sub>2</sub> CHNHC(O)	CH <sub>3</sub> C(O)	H	9.02	8.42
Table A101	Y	iPrNHC(O)	H	H	3.64	3.44
Table A102	Y	iPrNHC(O)	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	9.42	8.91
Table A103	Y	BuNHC(O)	H	H	4.21	3.95
Table A104	Y	CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> NHC(O)	H	H	3.44	3.25
Table A105	Y	BuNHC(O)	CH <sub>3</sub> C(O)	H	9.61	9.07
Table A106	Y	CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> NHC(O)	CH <sub>3</sub> C(O)	H	7.77	-
Table A107	Y	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>5</sub>		3.69	3.49
Table A108	Y	CH <sub>3</sub>	Br(CH <sub>2</sub> ) <sub>5</sub> OC(O)	H	11.08	10.61
Table A109	Y	CH <sub>3</sub>	tBuSO <sub>2</sub>	H	10.01	9.45
Table A110	Y	-CH <sub>2</sub> NHC(O)		CF <sub>3</sub> C(O)	12.85	12.53
Table A111	Y	Me <sub>3</sub> Si(CH <sub>2</sub> ) <sub>2</sub> NHC(O)	CF <sub>3</sub> C(O)	H	12.33	11.99
Table A112	Y	(CH <sub>2</sub> ) <sub>2</sub> CHNHC(O)	H	H	3.32	2.75
Table A113	Y	(CH <sub>2</sub> ) <sub>2</sub> CHNHC(O)	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	8.91	8.35
Table A114	Y	(CH <sub>2</sub> ) <sub>2</sub> CHNHC(O)	CH <sub>3</sub> C(O)	H	8.38	7.77
Table A115	Y	iPrNHC(O)	HC(O)	H	8.86	8.26
Table A116	Y	CH <sub>3</sub>	tBuOC(O)NH	H	9.86	9.31
Table A117	Y	HOCH <sub>2</sub> CH <sub>2</sub>	CH <sub>3</sub> C(O)	H	3.40	-
Table A118	Y	CN	BrCH <sub>2</sub> C(O)	H	9.23	-
Table A119	Y	HCC	PrC(O)	H	8.98	8.40
Table A120	Y	HCC	Et <sub>2</sub> CHC(O)	H	10.03	9.52
Table A121	Y	HCC	iPrC(O)	H	9.01	8.45
Table A122	Y	HCC	EtC(O)	H	8.36	7.74
Table A123	Y	HCC	(CH <sub>2</sub> ) <sub>2</sub> CHC(O)	H	8.80	8.22
Table A124	Y	HCC	CH <sub>3</sub> CHCHC(O)	H	8.81	8.22

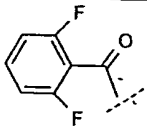
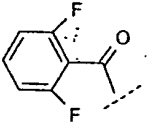
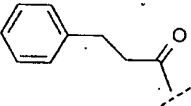
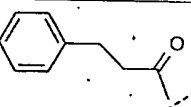
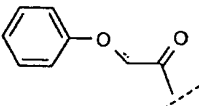
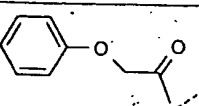
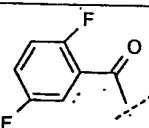
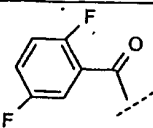
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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A125	Y	HCC	(CH <sub>2</sub> ) <sub>3</sub> CHC(O)	H	9.35	8.79
Table A126	Y	HCC	CH <sub>3</sub> CO <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(O)	H	9.08	8.49
Table A127	Y	HCC	EtOC(O)	H	9.17	8.62
Table A128	Y	HCC	tBuC(O)	H	9.82	9.30
Table A129	Y	HCC	iPrCH <sub>2</sub> C(O)	H	9.50	8.99
Table A130	Y	O <sub>2</sub> NCH <sub>2</sub>	H	H	4.11	3.84
Table A131	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> C(O)	H	8.67	8.08
Table A132	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	9.22	8.69
Table A133	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> CHCHC(O)	H	9.65	9.16
Table A134	Z	O <sub>2</sub> NCH <sub>2</sub>	EtC(O)	H	12.78	-
Table A135	Z	CH <sub>3</sub>	EtNHC(S)	H	13.13	12.70
Table A136	W	CH <sub>3</sub>	Propargyl	H	6.25	-
Table A137	Z	vinyl	HC(O)OCH <sub>2</sub> C(O)	H	11.95	11.27
Table A138	Z	CH <sub>3</sub>	HC(O)OCH <sub>2</sub> C(O)	H	11.46	10.71
Table A139	Z	CN	HC(O)OCH <sub>2</sub> C(O)	H	11.58	10.91
Table A140	Z	vinyl	H <sub>2</sub> NCH <sub>2</sub> C(O)	H	5.83	-
Table A141	Z	CH <sub>3</sub>	H <sub>2</sub> NCH <sub>2</sub> C(O)	H	5.49	5.12
Table A142	Z	CN	H <sub>2</sub> NCH <sub>2</sub> C(O)	H	5.56	5.06
Table A143	Z	vinyl	BrCH <sub>2</sub> C(O)	H	13.09	12.67
Table A144	Z	CH <sub>3</sub>	BrCH <sub>2</sub> C(O)	H	12.78	12.28
Table A145	A	CH <sub>3</sub>	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(O)	H	1.7	-
Table A146	A	CH <sub>3</sub>		H	-	2.0

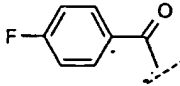
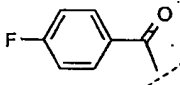
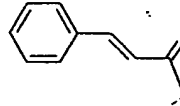
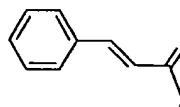
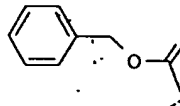
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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A147	A	CH <sub>3</sub>		H	2.2	-
Table A148	A	CH <sub>3</sub>		H	-	1.8
Table A149	A	CH <sub>3</sub>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> C(O)	H	-	2.2
Table A150	A	CH <sub>3</sub>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> C(O)	H	2.3	-
Table A151	A	CH <sub>3</sub>		H	-	2.1
Table A152	A	CH <sub>3</sub>		H	2.2	-
Table A153	A	CH <sub>3</sub>		H	-	2.1
Table A154	A	CH <sub>3</sub>		H	2.2	-
Table A155	A	CH <sub>3</sub>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> C(O)	H	2.4	-
Table A156	A	CH <sub>3</sub>		H	-	1.8
Table A157	A	CH <sub>3</sub>		H	1.9	-
Table A158	A	CH <sub>3</sub>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> C(O)	H	2.1	-

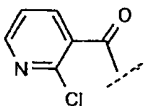
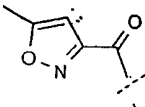
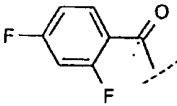
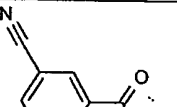
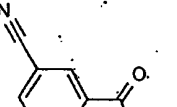
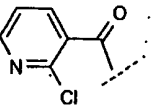
-133-

	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A159	A	CH <sub>3</sub>		H	-	1.87
Table A160	A	CH <sub>3</sub>		H	2	-
Table A161	A	CH <sub>3</sub>		H	-	1.96
Table A162	A	CH <sub>3</sub>		H	2.1	-
Table A163	A	CH <sub>3</sub>	CH <sub>2</sub> C(CH <sub>3</sub> )OCH <sub>2</sub> C(O)	H	-	1.5
Table A164	A	CH <sub>3</sub>	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub> C(O)	H	2.6	-
Table A165	A	CH <sub>3</sub>		H	-	2.0
Table A166	A	CH <sub>3</sub>		H	2.2	-
Table A167	A	CH <sub>3</sub>		H	-	2.0
Table A168	A	CH <sub>3</sub>		H	2.2	-

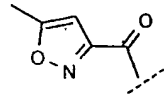
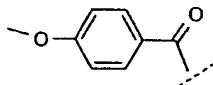
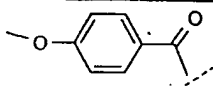
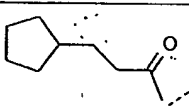
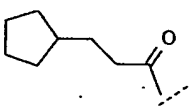
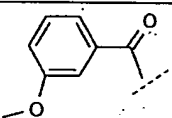
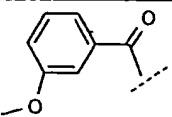
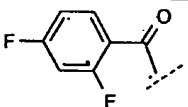
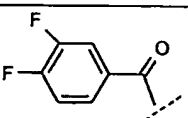
-134-

	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A169	A	CH <sub>3</sub>		H	-	1.9
Table A170	A	CH <sub>3</sub>		H	2.1	-
Table A171	A	CH <sub>3</sub>	BuOC(O)	H	2.3	-
Table A172	A	CH <sub>3</sub>	ClCH <sub>2</sub> CH <sub>2</sub> OC(O)	H	2.01	-
Table A173	A	CH <sub>3</sub>	CH <sub>2</sub> C(CH <sub>3</sub> )C(O)	H	2.1	-
Table A174	A	CH <sub>3</sub>		H	-	2.0
Table A175	A	CH <sub>3</sub>		H	2.0	-
Table A176	A	CH <sub>3</sub>	H <sub>2</sub> CCHCH <sub>2</sub> CH <sub>2</sub> OC(O)	H	2.2	-
Table A177	A	CH <sub>3</sub>		H	2.1	-
Table A178	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>2</sub> CCHC(O)	H	2.2	-
Table A179	Z	CH <sub>2</sub> NO <sub>2</sub>	PrC(O)	H	13.25	12.99
Table A180	Z	CH <sub>3</sub>	OH	H	7.00	6.44
Table A181	A	CH <sub>3</sub>	tBuC(O)	H	2.2	-
Table A182	A	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CCHC(O)	H	-	1.87
Table A183	A	CH <sub>3</sub>	Et <sub>2</sub> CHC(O)	H	2.2	-
Table A184	A	CH <sub>3</sub>	PhCH <sub>2</sub> C(O)	H	2.0	-
Table A185	A	CH <sub>3</sub>	iPrC(O)	H	1.9	-
Table A186	A	CH <sub>3</sub>	iPrCH <sub>2</sub> C(O)	H	2	-

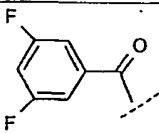
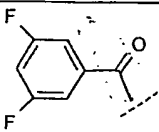
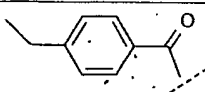
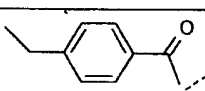
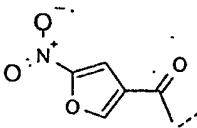
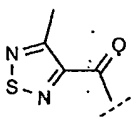
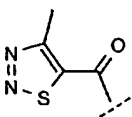
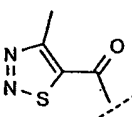
-135-

	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A187	A	CH <sub>3</sub>	EtC(O)	H	1.7	-
Table A188	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>2</sub> CHC(O)	H	1.8	-
Table A189	A	CH <sub>3</sub>		H	1.89	-
Table A190	A	CH <sub>3</sub>		H	-	1.9
Table A191	A	CH <sub>3</sub>	CH <sub>3</sub> CHCHC(O)	H	1.83	-
Table A192	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>3</sub> CHC(O)	H	2.0	-
Table A193	A	CH <sub>3</sub>		H	-	2.05
Table A194	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>4</sub> CHC(O)	H	2.3	-
Table A195	A	CH <sub>3</sub>	CH <sub>3</sub> CO <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(O)	H	1.9	-
Table A196	A	CH <sub>3</sub>		H	-	1.9
Table A197	A	CH <sub>3</sub>		H	2	-
Table A198	A	CH <sub>3</sub>	ClCH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> OC(O)	H	2.2	-
Table A199	A	CH <sub>3</sub>		H	-	1.69

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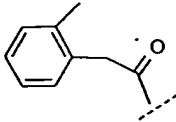
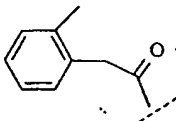
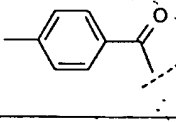
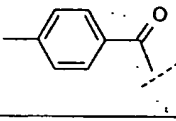
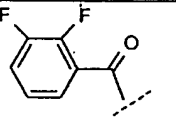
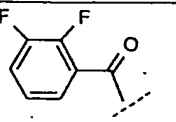
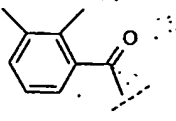
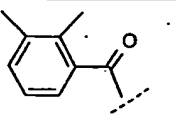
	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A200	A	CH <sub>3</sub>		H	2.1	-
Table A201	A	CH <sub>3</sub>		H	-	1.9
Table A202	A	CH <sub>3</sub>		H	2.1	-
Table A203	A	CH <sub>3</sub>		H	-	2.2
Table A204	A	CH <sub>3</sub>		H	2.3	-
Table A205	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>5</sub> CHC(O)	H	2.2	-
Table A206	A	CH <sub>3</sub>		H	-	1.9
Table A207	A	CH <sub>3</sub>		H	2.1	-
Table A208	A	CH <sub>3</sub>		H	2.2	-
Table A209	A	CH <sub>3</sub>		H	2.2	-

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	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A210	A	CH <sub>3</sub>		H	-	2.1
Table A211	A	CH <sub>3</sub>		H	2.2	-
Table A212	A	CH <sub>3</sub>		H	-	2.17
Table A213	A	CH <sub>3</sub>		H	2.3	-
Table A214	A	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>4</sub> CHC(O)	H	-	1.9
Table A215	A	CH <sub>3</sub>		H	2.0	-
Table A216	A	CH <sub>3</sub>		H	1.7	-
Table A217	A	CH <sub>3</sub>		H	-	1.8
Table A218	A	CH <sub>3</sub>		H	1.9	-
Table A219	A	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CH(CH <sub>2</sub> ) <sub>2</sub> C(O)	H	-	2.0
Table A220	A	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CH(CH <sub>2</sub> ) <sub>2</sub> C(O)	H	2.2	-



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	LC - MS	$R_a$	$R_b$	$R_c$	Retention time (min)	
					B1a	B1b
Table A221	A	CH <sub>3</sub>		H	-	2
Table A222	A	CH <sub>3</sub>		H	2.2	-
Table A223	A	CH <sub>3</sub>		H	-	2
Table A224	A	CH <sub>3</sub>		H	2.2	-
Table A225	A	CH <sub>3</sub>	PrC(O)	H	-	1.7
Table A226	A	CH <sub>3</sub>	CH <sub>3</sub> OC(O)(CH <sub>2</sub> ) <sub>4</sub> C(O)	H	1.8	-
Table A227	A	CH <sub>3</sub>		H	-	2.01
Table A228	A	CH <sub>3</sub>		H	2.2	-
Table A229	A	CH <sub>3</sub>	CH <sub>3</sub> S(CH <sub>2</sub> ) <sub>2</sub> C(O)	H	1.9	-
Table A230	A	CH <sub>3</sub>		H	-	2.1
Table A231	A	CH <sub>3</sub>		H	2.3	-
Table A232	A	CH <sub>3</sub>	Et <sub>2</sub> CHC(O)	H	-	2.0

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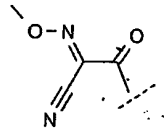
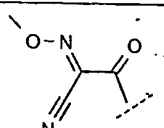
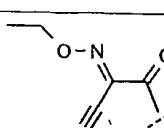
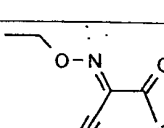
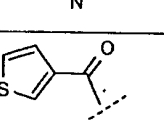
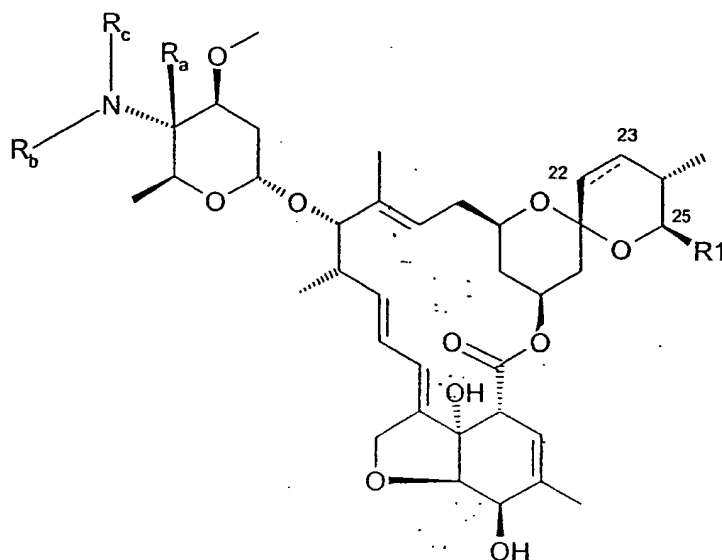
	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table A233	A	CH <sub>3</sub>		H	-	1.9
Table A234	A	CH <sub>3</sub>		H	2.0	-
Table A235	A	CH <sub>3</sub>		H	-	2.0
Table A236	A	CH <sub>3</sub>		H	2.2	-
Table A237	A	CH <sub>3</sub>		H	2.0	-
Table A238	A	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(O) )	H	-	1.72
Table A239	A	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(O) )	H	1.9	-
Table A240	A	CH <sub>3</sub>	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(O)	H	-	1.6

Table B: A compound of formula

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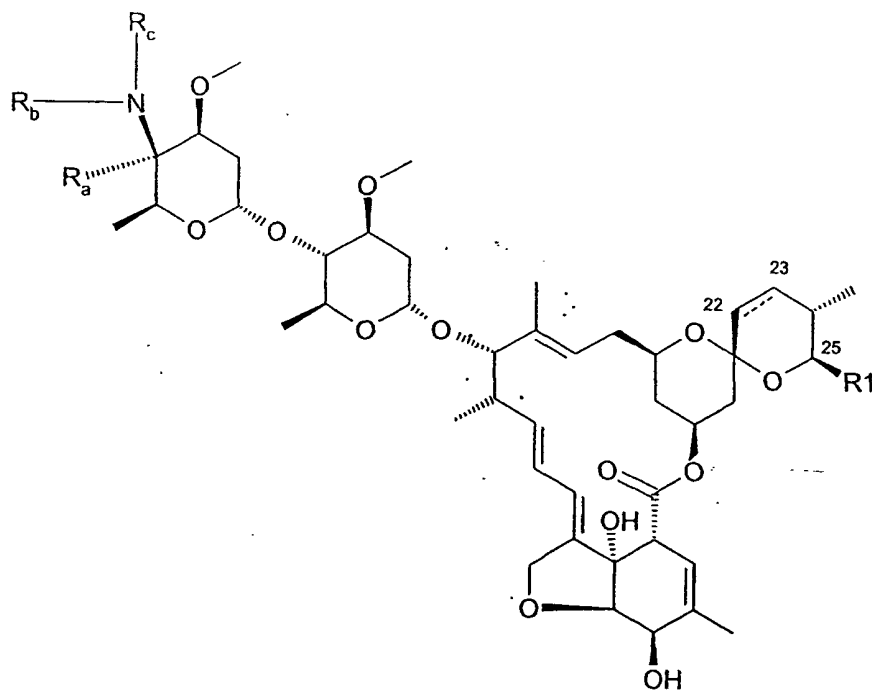
wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	$R_a$	$R_b$	$R_c$	Retention time (min)	
					B1a	B1b
Table B1	W	CH <sub>3</sub>	H	H	4.71	4.46
Table B2	W	vinyl	H	H	4.94	4.71
Table B3	W	allyl	H	H	5.71	-
Table B4	W	vinyl	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	10.03	-
Table B5	W	vinyl	CH <sub>3</sub> C(O)	H	8.85	8.00
Table B6	Z	vinyl	allyl	H	3.75	3.38
Table B7	Z	allyl	allyl	H	5.00	-
Table B8	Z	vinyl	Propargyl	H	5.70	5.06
Table B9	Z	Allyl	Propargyl	H	6.01	5.41
Table B10	Z	CN	CH <sub>3</sub>	OH	10.34	9.63
Table B11	Z	O <sub>2</sub> NCH <sub>2</sub>	H	H	5.10	4.7
Table B12	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> C(O)	H	9.93	9.22
Table B13	Z	O <sub>2</sub> NCH <sub>2</sub>	PrC(O)	H	11.83	-

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	LC-MS	$R_a$	$R_b$	$R_c$	Retention time (min)	
					B1a	B1b
Table B14	Z	$O_2NCH_2$	$CH_3OCH_2C(O)$	H	10.95	10.31
Table B15	Z	$O_2NCH_2$	$iPrC(O)$	H	11.94	11.28
Table B16	Z	$O_2NCH_2$	$CH_3OC(O)$	H	13.01	12.66
Table B17	Z	$O_2NCH_2$	$iPrCH_2C(O)$	H	12.46	11.98
Table B18	Z	$O_2NCH_2$	$EtC(O)$	H	10.97	10.30
Table B19	Z	$O_2NCH_2$	$(CH_2)_2CHC(O)$	H	11.41	10.75
Table B20	Z	$O_2NCH_2$	$CH_3CHCH_2C(O)$	H	11.55	10.87

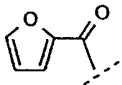
Table C: A compound of formula



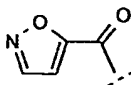
wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22  
 5 and 23 is a double bond, and

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	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table C1	W	CH <sub>3</sub>	H	H	4.53	4.16
Table C2	W	vinyl	H	H	5.42	5.12
Table C3	W	Allyl	H	H	5.60	5.33
Table C4	W	PhCH <sub>2</sub>	H	H	6.03	5.81
Table C5	W	HCC	H	H	5.32	5.07
Table C6	W	Ph	H	H	6.13	5.87
Table C7	W	CH <sub>3</sub>	CH <sub>3</sub> C(O)	H	9.82	9.01
Table C8	W	vinyl	CH <sub>3</sub> C(O)	H	10.04	9.24
Table C9	W	Allyl	CH <sub>3</sub> C(O)	H	10.24	-
Table C10	W	HCC	CH <sub>3</sub> C(O)	H	9.13	-
Table C11	W	PhCH <sub>2</sub>	CH <sub>3</sub> C(O)	H	11.44	10.68
Table C12	X	PhCH <sub>2</sub>	HC(O)	H	15.44	-
Table C13	W	CH <sub>3</sub>	HC(O)	H	9.74	-
Table C14	W	vinyl	HC(O)	H	10.35	-
Table C15	W	Allyl	HC(O)	H	10.72	-
Table C16	W	HCC	HC(O)	H	9.43	-
Table C17	W	HCC	CH <sub>3</sub> OC(O)	H	10.30	-
Table C18	W	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H	11.57	-
Table C19	W	HCC	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H	10.94	-
Table C20	W	HCC	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	10.03	-
Table C21	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> C(O)	H	11.28	-
Table C22	Z	CH <sub>3</sub>	CH <sub>3</sub> CH <sub>2</sub> OCH <sub>2</sub> C(O)	H	12.39	11.78
Table C23	W	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	6.61	6.19
Table C24	W	HCC	CH <sub>3</sub>	CH <sub>3</sub>	5.87	5.65
Table C25	W	vinyl	allyl	H	6.08	5.76
Table C26	W	allyl	allyl	H	6.67	-

	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table C27	Y	CH <sub>3</sub>	Propargyl	H	6.24	-
Table C28	W	Allyl	Propargyl	H	6.26	-
Table C29	W	CH <sub>3</sub>	allyl	H	6.40	5.98
Table C30	Z	CH <sub>3</sub>	CH <sub>3</sub>	H	4.86	-
Table C31	Z	CH <sub>3</sub>	CH <sub>3</sub>	OH	5.78	-
Table C32	Z	CH <sub>3</sub>	OC(O)CH <sub>3</sub>	CH <sub>3</sub>	12.95	12.50
Table C33	W	CN	H	H	8.25	7.62
Table C34	U	CN	CH <sub>3</sub> C(O)	H	8.12	7.50
Table C35	W	CN	CH <sub>3</sub>	H	8.76	8.6
Table C36	W	CN	CH <sub>3</sub> CH <sub>2</sub> C(O)	H	9.37	8.72
Table C37	W	CN	CH <sub>3</sub> OC(O)	H	9.74	9.04
Table C38	W	CN	(CH <sub>2</sub> CH <sub>2</sub> )CHC(O)	H	9.65	8.96
Table C39	W	CN	CH <sub>3</sub> CH <sub>2</sub> OC(O)	H	9.60	9.02
Table C40	W	CN	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	10.01	9.28
Table C41	W	CN	CH <sub>2</sub> CHCH <sub>2</sub> OC(O)	H	10.52	9.87
Table C42	W	CN	tBuC(O)	H	11.25	10.59
Table C43	W	CN	iPrCH <sub>2</sub>	H	10.48	9.79
Table C44	W	CN	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OC(O)	H	10.99	10.37
Table C45	W	CN		H	10.56	9.87
Table C46	W	CN	CH <sub>2</sub> CHCH <sub>2</sub> CH <sub>2</sub> OC(O)	H	10.98	10.38
Table C47	W	CN	Et <sub>2</sub> CHC(O)	H	11.08	10.46
Table C48	W	CN	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> C(O)	H	10.95	10.34
Table C49	W	CN	CH <sub>3</sub> C(O)OCH <sub>2</sub> C(O)	H	9.14	8.47
Table C50	W	CN	CH <sub>3</sub> OC(O)CH <sub>2</sub> C(O)	H	9.67	9.02
Table C51	W	CN	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> OC(O)	H	11.48	10.88

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	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table C52	W	CN	ClCH <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> C(O)	H	9.74	9.14
Table C53	W	CN	CyclohexylC(O)	H	11.31	10.68
Table C54	W	CN	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> C(O)	H	11.54	10.96
Table C55	W	CN	m-CH <sub>3</sub> PhC(O)	H	11.19	10.58
Table C56	W	CN	PhCH <sub>2</sub> C(O)	H	10.17	9.50
Table C57	W	CN	ClCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(O)	H	10.54	-
Table C58	W	CN	ClCH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> C(O)	H	9.30	-
Table C59	W	CN	p-FPhC(O)	H	10.77	10.15
Table C60	W	CN	m-FPhC(O)	H	10.72	10.07
Table C61	W	CN	o-FPhC(O)	H	11.27	10.64
Table C62	W	CN	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub> C(O)	H	12.07	11.52
Table C63	W	CN	EtOC(O) (CH <sub>2</sub> ) <sub>2</sub> C(O)	H	9.55	8.90
Table C64	W	CN	HC(O)	H	8.30	7.68
Table C65	W	CN	Bu	H	12.58	12.05
Table C66	W	CN	tBuCH <sub>2</sub>	H	13.77	13.13
Table C67	W	CN	(CH <sub>2</sub> CH <sub>2</sub> )CHGH <sub>2</sub>	H	12.59	12.00
Table C68	W	CN	CH <sub>3</sub> CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>3</sub>	H	12.11	-
Table C69	W	CN	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	H	12.78	12.16
Table C70	W	CN	iPrC(O)	H	10.10	9.41
Table C71	W	CN	iPrOC(O)	H	10.63	-
Table C72	W	CN	ClCH <sub>2</sub> CH <sub>2</sub> C(O)	H	9.70	9.05
Table C73	W	CN		H	10.03	9.36
Table C74	W	CN	tBuCH <sub>2</sub> C(O)	H	11.12	10.49
Table C75	W	CN	Et <sub>2</sub> NC(O)	H	-	-

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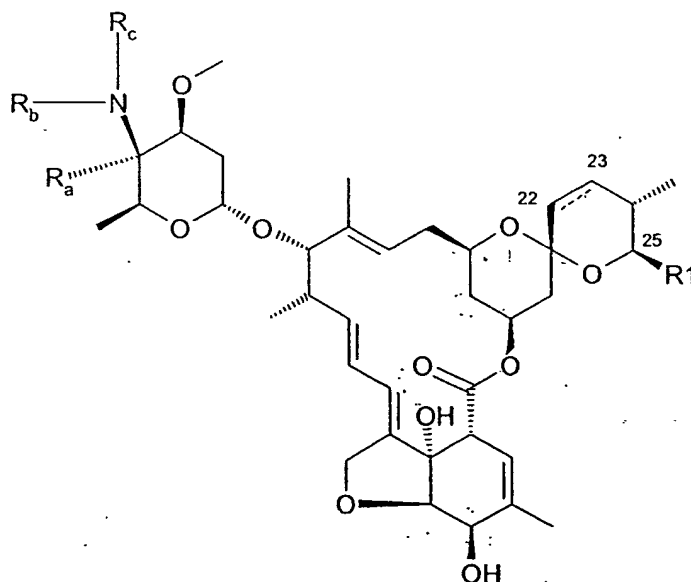
	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table C76	W	CN		H	10.73	-
Table C77	W	CN	o-CH <sub>3</sub> PhC(O)	H	11.02	10.47
Table C78	W	CN	PhOC(O)	H	10.88	10.28
Table C79	Z	CH <sub>3</sub>	FCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	13.21	12.8
Table C80	Z	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	13.51	13.18
Table C81	Z	CH <sub>3</sub>	EtCO <sub>2</sub>	CH <sub>3</sub>	13.41	13.05
Table C82	Z	CH <sub>3</sub>	iPrCO <sub>2</sub>	CH <sub>3</sub>	13.73	13.42
Table C83	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.81	12.30
Table C84	Z	CH <sub>3</sub>	tBuCO <sub>2</sub>	CH <sub>3</sub>	13.97	13.70
Table C85	Z	CH <sub>3</sub>	CH <sub>3</sub> OC(O)CH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.88	12.47
Table C86	Z	CH <sub>3</sub>	Cl <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	13.92	-
Table C87	Z	CN	FCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.91	12.55
Table C88	Z	CN	(CH <sub>2</sub> ) <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	13.28	12.96
Table C89	Z	CN	iPrCO <sub>2</sub>	CH <sub>3</sub>	13.51	13.23
Table C90	Z	CN	CH <sub>3</sub> OCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.69	12.27
Table C91	Z	CN	tBuCO <sub>2</sub>	CH <sub>3</sub>	13.73	13.49
Table C92	Z	CN	Cl <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	13.68	13.44
Table C93	Z	CN	CH <sub>3</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.84	12.44
Table C94	Z	CN	CH <sub>3</sub> OCO <sub>2</sub>	CH <sub>3</sub>	13.02	12.67
Table C95	Z	CN	CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.78	12.04
Table C96	Z	CN	OH	CH <sub>3</sub>	11.98	-
Table C97	Z	vinyl	CH <sub>3</sub> CO <sub>2</sub>	CH <sub>3</sub>	13.23	12.86
Table C98	Z	vinyl	CH <sub>3</sub> OCO <sub>2</sub>	CH <sub>3</sub>	13.32	12.96
Table C99	Z	vinyl	FCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	13.40	13.09
Table C100	Z	vinyl	(CH <sub>2</sub> ) <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	13.65	13.34

	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table C101	Z	vinyl	iPrCO <sub>2</sub>	CH <sub>3</sub>	13.87	13.58
Table C102	Z	vinyl	tBuCO <sub>2</sub>	CH <sub>3</sub>	14.12	13.86
Table C103	Z	vinyl	(CH <sub>2</sub> ) <sub>4</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	14.28	14.04
Table C104	Z	vinyl	PhCO <sub>2</sub>	CH <sub>3</sub>	14.13	13.87
Table C105	Z	vinyl	OH	CH <sub>3</sub>	7.12	6.54
Table C106	Z	vinyl	Me <sub>2</sub> NCO <sub>2</sub>	CH <sub>3</sub>	12.88	-
Table C107	Z	vinyl	OH	Allyl	12.02	11.35
Table C108	Z	CH <sub>3</sub>	OH	Allyl	9.10	-
Table C109	Z	vinyl	OH	H	8.33	7.66
Table C110	Z	CH <sub>3</sub>	OH	H	5.99	-
Table C111	Y	CH <sub>3</sub> CC	CH <sub>3</sub> C(O)	H	7.96	7.36
Table C112	Y	CH <sub>3</sub> OCH <sub>2</sub> CC	CH <sub>3</sub> C(O)	H	7.58	-
Table C113	Y	CH <sub>3</sub> CC	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	8.81	8.21
Table C114	Y	CN	CH <sub>3</sub>	H	9.16	8.63
Table C115	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub>	H	3.59	3.36
Table C116	Y	CH <sub>3</sub>	CH <sub>3</sub>	Allyl	3.75	3.55
Table C117	Y	CH <sub>3</sub>	CH <sub>3</sub>	Allyl	3.70	3.50
Table C118	Y	CN	BrCH <sub>2</sub> C(O)	H	9.04	8.51
Table C119	Y	O <sub>2</sub> NCH <sub>2</sub>	H	H	3.80	3.59
Table C120	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> C(O)	H	8.44	-
Table C121	Y	O <sub>2</sub> NCH <sub>2</sub>	PrC(O)	H	9.80	9.31
Table C122	Y	O <sub>2</sub> NCH <sub>2</sub>	(CH <sub>2</sub> ) <sub>2</sub> CHC(O)	H	9.50	9.00
Table C123	Y	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> CHCHC(O)	H	9.57	9.07
Table C124	Z	CN	HC(O)CH <sub>2</sub> C(O)	H	11.31	10.65
Table C125	Z	CN	H <sub>2</sub> NCH <sub>2</sub> C(O)	H	5.18	-
Table C126	Z	CN	HC(O)	CH <sub>3</sub>	10.53	9.89

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	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
		22-23-dihydro				
Table C127	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	11.95	11.23
Table C128	Z	-CH <sub>2</sub> CH <sub>2</sub> OSO <sub>2</sub> -		H	12.80	-
Table C129	Y	-CH <sub>2</sub> CH <sub>2</sub> OC(Ph)		-	6.50	-
Table C130	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)O	H	14.20	13.78
Table C131	Z	CH <sub>3</sub>	CH <sub>3</sub> C(O)O	H	12.79	12.34
Table C132	W	CH <sub>3</sub>	Allyl	H	6.03	5.66

Table D: A compound of formula



wherein R<sub>1</sub> is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)
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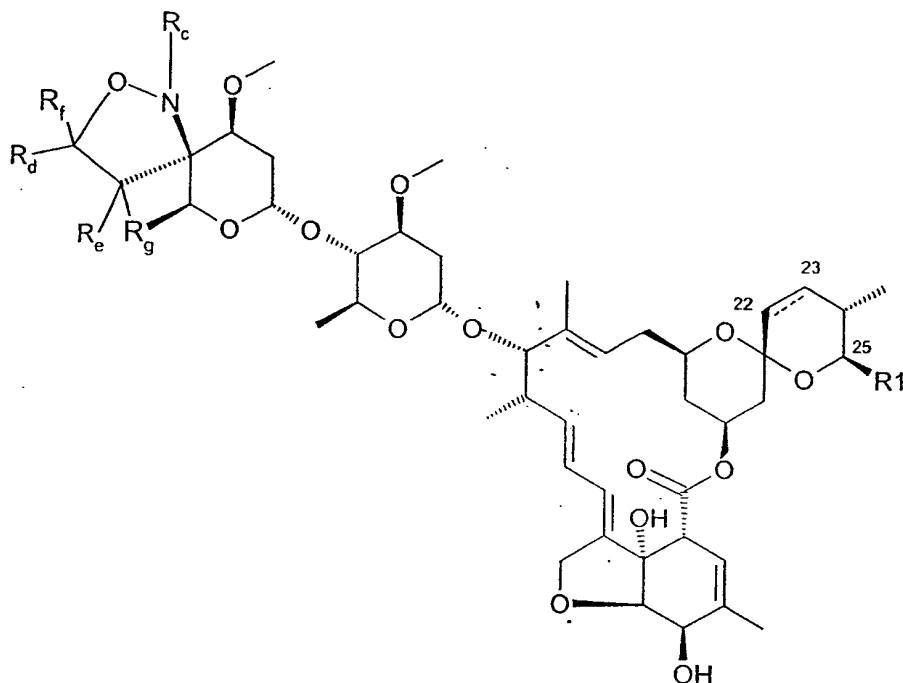
					B1a	B1b
Table D1	W	CH <sub>3</sub>	H	H	3.95	-
Table D2	W	vinyl	H	H	4.06	-
Table D3	W	Allyl	H	H	5.71	-
Table D4	W	CH <sub>3</sub>	CH <sub>3</sub> C(O)	H	8.7	7.90
Table D5	W	CH <sub>3</sub>	HC(O)	H	8.54	7.74
Table D6	W	vinyl	CH <sub>3</sub> C(O)	H	7.04	-
Table D7	W	vinyl	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	8.31	-
Table D8	W	vinyl	CH <sub>3</sub> OC(O)	H	8.64	-
Table D9	W	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	9.56	8.70
Table D10	W	Allyl	CH <sub>3</sub> OC(O)	H	9.43	8.71
Table D11	W	Allyl	CH <sub>3</sub> C(O)	H	7.70	-
Table D12	Z	vinyl	allyl	H	3.75	-
Table D13	W	allyl	allyl	H	4.55	-
Table D14	Z	vinyl	Propargyl	H	6.19	-
Table D15	Z	Allyl	Propargyl	H	5.09	-
Table D16	W	CN	H	H	7.36	6.66
Table D17	W	CN	CH <sub>3</sub>	H	8.39	8.05
Table D18	Z	CH <sub>3</sub>	FCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	12.24	11.69
Table D19	Z	CH <sub>3</sub>	(CH <sub>2</sub> ) <sub>2</sub> CHCO <sub>2</sub>	CH <sub>3</sub>	12.68	12.19
Table D20	Z	CH <sub>3</sub>	iPrCO <sub>2</sub>	CH <sub>3</sub>	13.05	12.65
Table D21	Z	CH <sub>3</sub>	tBuCO <sub>2</sub>	CH <sub>3</sub>	13.37	13.05
Table D22	Z	CH <sub>3</sub>	CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.71	11.07
Table D23	Z	CH <sub>3</sub>	CH <sub>3</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.87	11.16
Table D24	Z	CH <sub>3</sub>	CH <sub>3</sub> OCO <sub>2</sub>	CH <sub>3</sub>	12.18	11.54
Table D25	Z	CH <sub>3</sub>	CH <sub>3</sub> OCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.57	10.91
Table D26	Z	CH <sub>3</sub>	Cl <sub>2</sub> HCCO <sub>2</sub>	CH <sub>3</sub>	13.34	13.12
Table D27	Z	CN	CH <sub>3</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.57	10.91
Table D28	Z	CN	CH <sub>3</sub> OCO <sub>2</sub>	CH <sub>3</sub>	11.92	11.31

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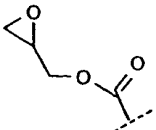
	LC - MS	R <sub>a</sub>	R <sub>b</sub>	R <sub>c</sub>	Retention time (min)	
					B1a	B1b
Table D29	Z	CN	CH <sub>3</sub> OCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.30	10.67
Table D30	Z	CN	FCH <sub>2</sub> CO <sub>2</sub>	CH <sub>3</sub>	11.76	11.20
Table D31	Z	O <sub>2</sub> NCH <sub>2</sub>	H	H	4.94	4.53
Table D32	Z	O <sub>2</sub> NCH <sub>2</sub>	PrC(O)	H	12.13	11.55
Table D33	Z	O <sub>2</sub> NCH <sub>2</sub>	(CH <sub>2</sub> ) <sub>2</sub> CHC(O)	H	11.86	11.22
Table D34	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> CHCHC(O)	H	11.91	11.28
Table D35	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> C(O)	H	10.65	9.86
Table D36	Z	O <sub>2</sub> NCH <sub>2</sub>	IPrCH <sub>2</sub> C(O)	H	12.61	12.16
Table D37	Z	O <sub>2</sub> NCH <sub>2</sub>	EtC(O)	H	11.49	-
Table D38	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> OCH <sub>2</sub> C(O)	H	11.41	-
Table D39	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub> OC(O)	H	11.92	11.26
Table D40	Z	O <sub>2</sub> NCH <sub>2</sub>	iPrC(O)	H	12.20	11.63
Table D41	Z	O <sub>2</sub> NCH <sub>2</sub>	Et <sub>2</sub> CHC(O)	H	13.03	12.65
Table D42	Z	O <sub>2</sub> NCH <sub>2</sub>	CH <sub>3</sub>	H	4.70	4.30

Table E: A compound of formula

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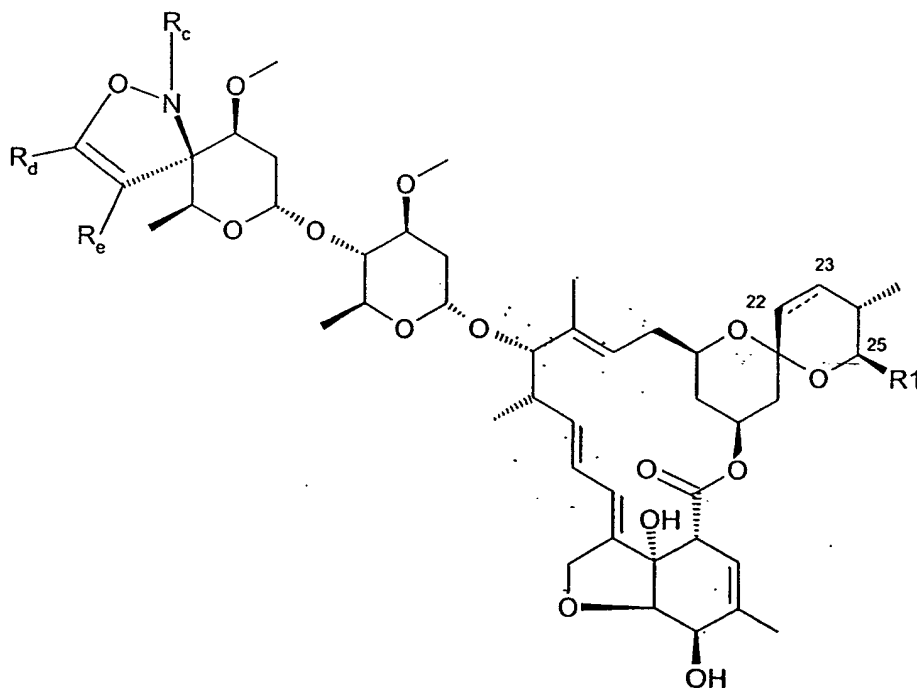
wherein R<sub>1</sub> is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R <sub>c</sub>	R <sub>d</sub>	R <sub>e</sub>	R <sub>f</sub>	R <sub>g</sub>	Retention time (min)	
							B1a	B1b
Table E1	Z	CH <sub>3</sub>	CO <sub>2</sub> CH <sub>3</sub>	H	H	H	14.78	-
Table E2	Z	CH <sub>3</sub>	CO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	H	H	H	12.75	-
Table E3	Z	CH <sub>3</sub>		H	H	H	12.06	11.39
Table E4	Z	CH <sub>3</sub>	CO <sub>2</sub> tBu	H	H	H	13.39 13.49	13.06 13.17
Table E5	Z	CH <sub>3</sub>	PhSO <sub>2</sub>	H	H	H	13.27 13.17	- 12.80

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	LC-MS	R <sub>c</sub>	R <sub>d</sub>	R <sub>e</sub>	R <sub>f</sub>	R <sub>g</sub>	Retention time (min)	
							B1a	B1b
Table E6	Z	CH <sub>3</sub>	OEt	H	H	H	12.32	-
							11.80	-
Table E7	Z	CH <sub>3</sub>	CH <sub>2</sub> OC(O)CH <sub>3</sub>	H	H	H	11.67	-
							11.19	-
Table E8	Z	CH <sub>3</sub>	CN	H	H	H	12.89	12.43
							12.70	12.22
Table E9	Z	CH <sub>3</sub>	o-FPh	H	H	H	13.51	13.22
							-	-

Table F: A compound of formula

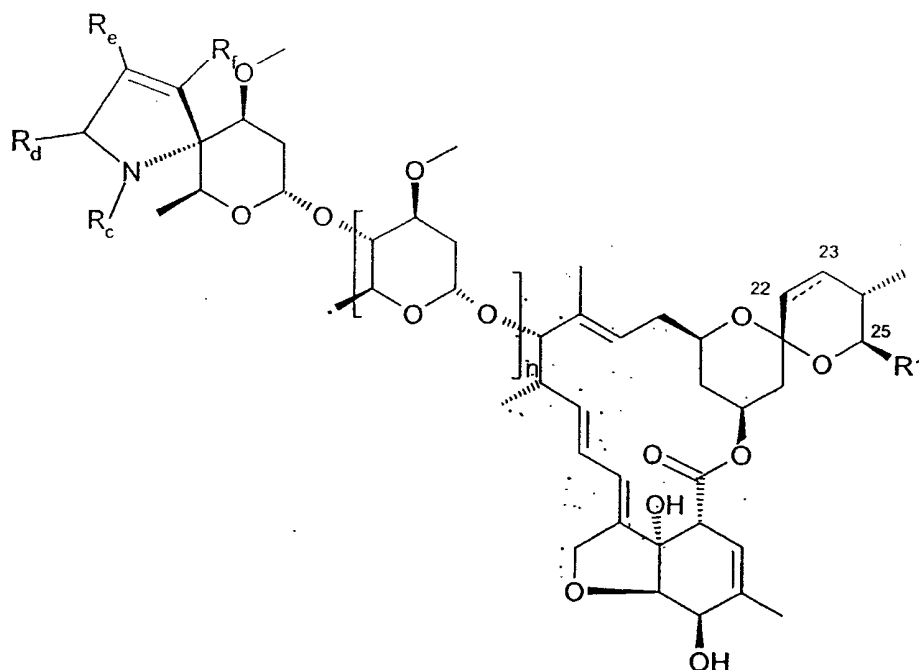


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wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	$R_c$	$R_d$	$R_e$	Retention time (min)	
					B1a	B1b
Table F1	Z	C(O)OMe	C(O)OMe	CH <sub>3</sub>	13.34	13.02

Table G: A compound of formula



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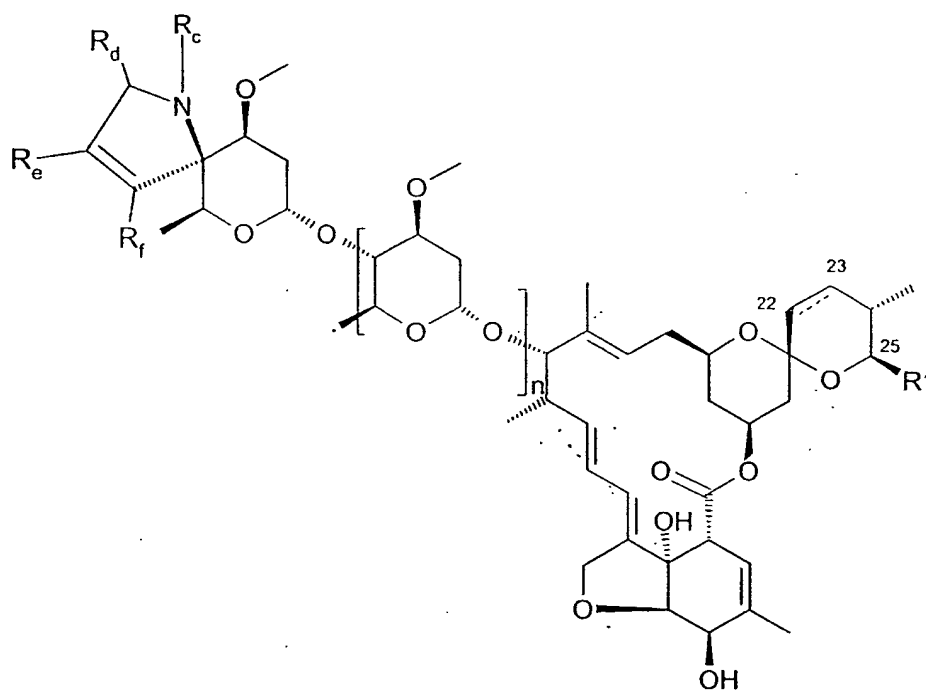
wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	n	$R_c$	$R_d$	$R_e$	$R_f$	Retention time (min)	
							B1a	B1b
Table G1	W	1	H	H	H	H	9.57	



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Table G2	Z	0	H	H	H	H	3.94	-
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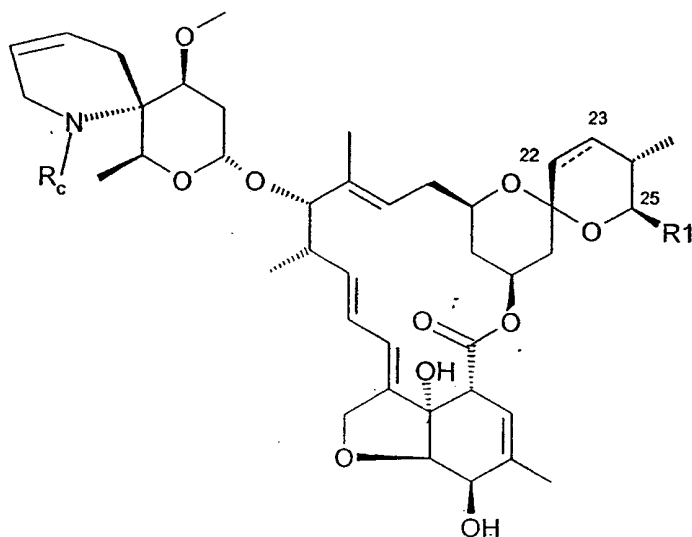
Table H: A compound of formula

wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22  
 5 and 23 is a double bond, and

		n	R <sub>c</sub>	R <sub>c</sub>	R <sub>c</sub>	R <sub>f</sub>	Retention time (min)	
	LC-MS						B1a	B1b
Table H1	W	1	H	H	H	H	9.87	-
Table H2	Z	0	H	H	H	H	3.47	-

Table I: A compound of formula

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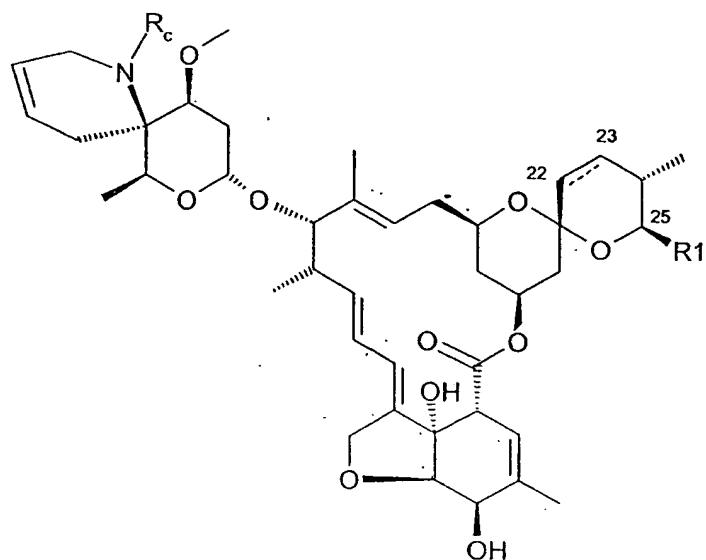


wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		$R_c$	Retention time (min)	
			B1a	B1b
Table I1	Z	H	4.49	-

5 Table J: A compound of formula

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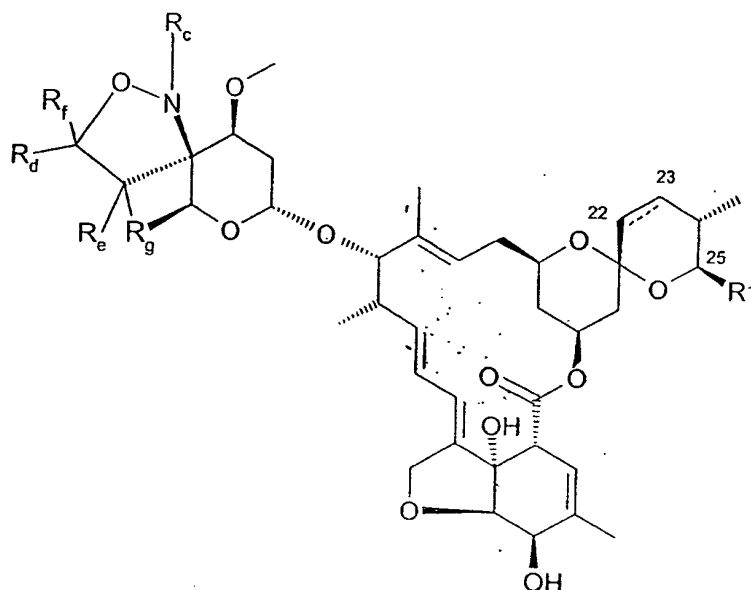


wherein  $R_1$  is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

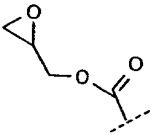
		$R_4$	Retention time (min)	
			B1a	B1b
Table J1	Z	H	3.62-3.45	-

5 Table K: A compound of formula

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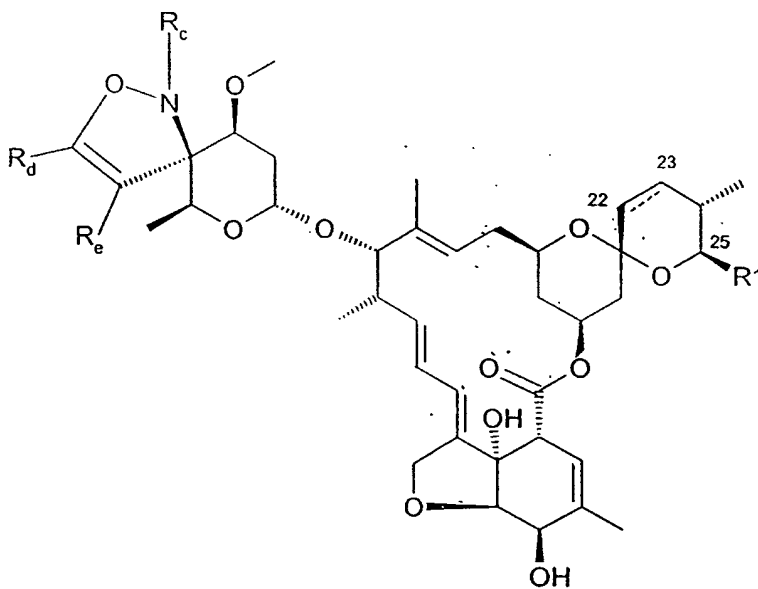
wherein R<sub>1</sub> is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R <sub>c</sub>	R <sub>d</sub>	R <sub>e</sub>	R <sub>f</sub>	R <sub>g</sub>	Retention time (min)	
							B1a	B1b
Table K1	Z	CH <sub>3</sub>	CO <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	H	H	H	11.16 11.46	10.39 -
Table K2	Z	CH <sub>3</sub>		H	H	H	10.14 10.44	10.39 -
Table K3	Z	CH <sub>3</sub>	CN	H	H	H	11.70 11.32	10.93 -
Table K4	Z	CH <sub>3</sub>	OEt	H	H	H	10.82 9.88	- -
Table K5	Z	CH <sub>3</sub>	CH <sub>2</sub> OC(O)CH <sub>3</sub>	H	H	H	9.75 9.29	- -

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Table K6	Z	CH <sub>3</sub>	o-FPh	H	H	H	12.77	12.27
Table K7	Z	CH <sub>3</sub>	PhSO <sub>2</sub>	H	H	H	12.20	11.49
							12.34	11.75

Table L: A compound of formula



wherein R<sub>1</sub> is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		R <sub>c</sub>	R <sub>d</sub>	R <sub>e</sub>	Retention time (min)	
					B1a	B1b
Table L1	Z	C(O)OMe	C(O)OMe	CH <sub>3</sub>	12.52	11.98

Also made available are compounds having the following characteristics:

Table M1	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is cyclohexyl.
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Table M2	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is 1-methyl butyl.
Table M3	A compound corresponding to a line of Tables A to J, wherein the bond between the carbon atoms 22 and 23 is a single bond.
Table M4	A compound corresponding to a line of Tables A to J, wherein the configuration of the carbon atom at the $\epsilon$ position is opposite of that represented.
Table M5	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is cyclohexyl and the bond between the carbon atoms 22 and 23 is a single bond.
Table M6	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is 1-methyl butyl and the bond between the carbon atoms 22 and 23 is a single bond.
Table M7	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is cyclohexyl, the bond between the carbon atoms 22 and 23 is a single bond and the configuration of the carbon atom at the $\epsilon$ position is opposite of that represented.
Table M8	A compound corresponding to a line of Tables A to J, wherein R <sub>1</sub> is 1-methyl butyl, the bond between the carbon atoms 22 and 23 is a single bond and the configuration of the carbon atom at the $\epsilon$ position is opposite of that represented.

Biological Examples:Example B1: Activity against Spodoptera littoralis

- Young soya bean plants are sprayed with an aqueous emulsion spray liquor which
- 5 comprises 12.5 ppm of active compound, and, after the spray coating has dried on, populated with 10 caterpillars of the first stage of *Spodoptera littoralis* and introduced into a plastic container. 3 days later, the reduction in the population in percent and the reduction in the feeding damage in per cent (% activity) are determined by comparing the number of dead caterpillars and the feeding damage between the treated and the untreated plants.
- 10 In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B2: Activity against *Spodoptera littoralis*, systemic:

Maize seedlings are placed into the test solution which comprises 12.5 ppm of active compound. After 6 days, the leaves are cut off, placed onto moist filter paper in a Petri dish and populated with 12 to 15 *Spodoptera littoralis* larvae of the L<sub>1</sub> stage. 4 days later, the  
5 reduction of the population in per cent (% activity) is determined by comparing the number of dead caterpillars between the treated and the untreated plants.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6,  
10 Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B3: Activity against *Heliothis virescens*

35 0- to 24-hour-old eggs of *Heliothis virescens* are placed onto filter paper in a Petri dish on a layer of synthetic feed. 0.8 ml of the test solution which comprises 12.5 ppm of active  
15 compound, is then pipetted onto the filter papers. Evaluation is carried out after 6 days. The reduction in the population in per cent (% activity) is determined by comparing the number of dead eggs and larvae on the treated and the untreated filter papers.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table  
20 A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B4: Activity against *Plutella xylostella* caterpillars

Young cabbage plants are sprayed with an aqueous emulsion spray liquor which comprises  
25 12.5 ppm of the active compound. After the spray coating has dried on, the cabbage plants are populated with 10 caterpillars of the first stage of *Plutella xylostella* and introduced into a plastic container. Evaluation is carried out after 3 days. The reduction in the population in per cent and the reduction in the feeding damage in per cent (% activity) are determined by

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comparing the number of dead caterpillars and the feeding damage on the treated and the untreated plants.

- In this test, the compounds of formulae (I), (III) and (V) show good activity against *Plutella xylostella*. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B5: Activity against *Frankliniella occidentalis*

- 10 In Petri dishes, discs of the leaves of beans are placed onto agar and sprayed with test solution which comprises 12.5 ppm of active compound, in a spraying chamber. The leaves are then populated with a mixed population of *Frankliniella occidentalis*. Evaluation is carried out after 10 days. The reduction in per cent (% activity) is determined by comparing the population on the treated leaves with that of the untreated leaves.
- 15 In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

20 Example B6: Activity against *Diabrotica balteata*

- Maize seedlings are sprayed with an aqueous emulsion spray liquor which comprises 12.5 ppm of active compound and, after the spray coating has dried on, populated with 10 larvae of the second stage of *Diabrotica balteata* and then introduced into a plastic container. After 6 days, the reduction in the population in per cent (% activity) is determined by comparing the dead larvae between the treated and the untreated plants.

In this test, compounds of formula (I), (III), and (V) show good activity, in particular, the compound from Table A8, Table A9, Table A11, Table A12, Table C23.



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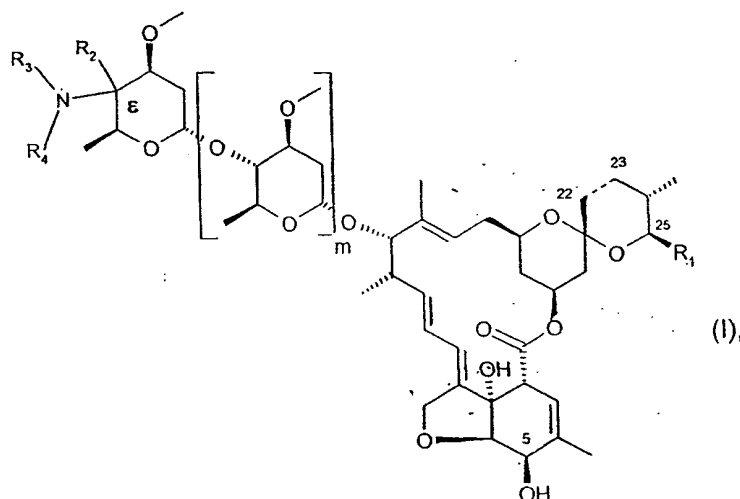
Example B7: Activity against Tetranychus urticae

Young bean plants are populated with a mixed population of Tetranychus urticae and, after 1 day, sprayed with an aqueous emulsion spray-liquor which comprises 12.5 ppm of active compound, incubated at 25°C for 6 days and then evaluated. The reduction in the  
5 population in per cent (% activity) is determined by comparing the number of dead eggs, larvae and adults on the treated and on the untreated plants.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6,  
10 Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

## CLAIMS

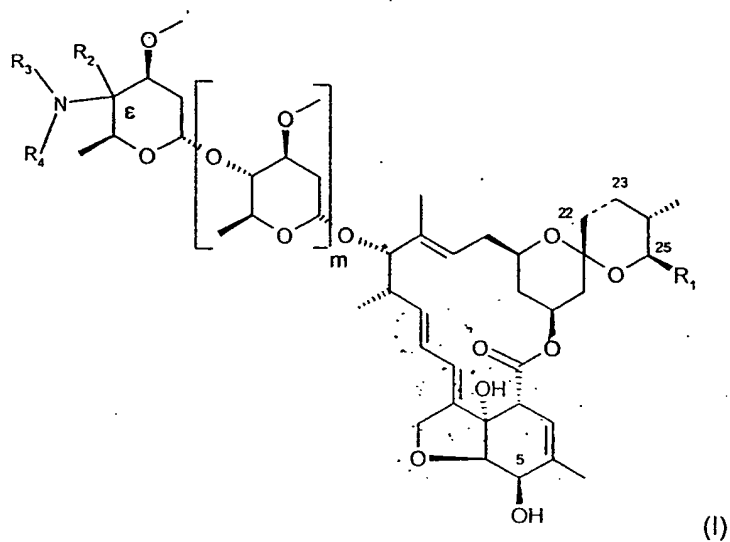
1. A compound of the formula (I)



- 5 wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,
- m is 0 or 1,
- R<sub>1</sub> represents a C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl group,
- R<sub>2</sub> represents a hydrocarbyl group or a substituted hydrocarbyl group, and
- 10 R<sub>3</sub> and R<sub>4</sub> represent, independently of each other, hydrogen or a chemical constituent, or either R<sub>2</sub> and R<sub>3</sub> together or R<sub>3</sub> and R<sub>4</sub> together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH<sub>2</sub> group may be replaced by O, S or NR<sub>6</sub>, where R<sub>6</sub> represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer
- 15 and/or tautomer of the compound of formula (I), in each case in free form or in salt form.

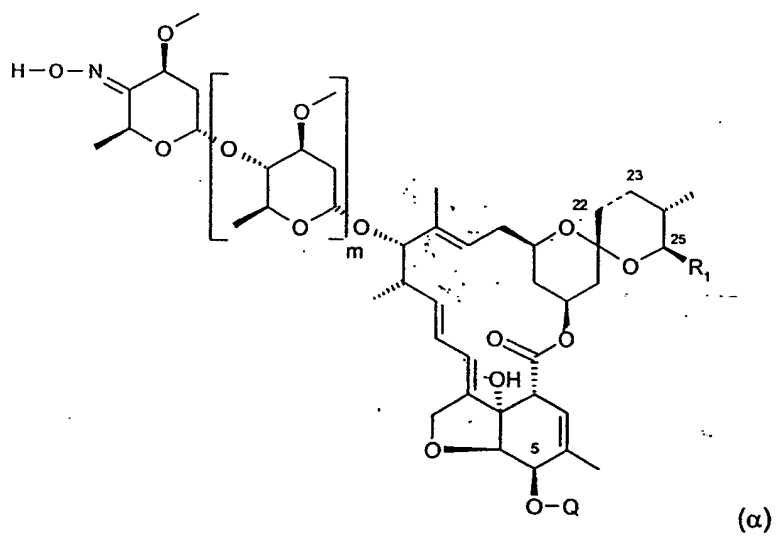
2. A process for preparing a compound of formula (I)

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wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, comprising the steps of:

- 5 (i) synthesizing a compound of formula ( $\alpha$ )



wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in claim 1 and Q is a protecting group;

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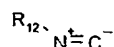
(ii) reacting a disulfide, an aliphatic or aromatic phosphine and a compound of formula ( $\alpha$ ) to yield a sulfenimine derivative of the compound of formula ( $\alpha$ );

5 (iii) oxidising the sulfenimine derivative of the compound of formula ( $\alpha$ ) to yield a sulfinimine derivative of the compound of formula ( $\alpha$ );

either

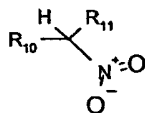
(iva) reacting an organometallic reagent having the  $R_2$  group with the sulfinimine derivative of the compound of formula ( $\alpha$ ) to yield a desoxy - sulfinamide - hydrocarbyl derivative of the compound of formula ( $\alpha$ ); or

10 (ivb) reacting an isocyanate reagent of formula



where  $R_{12}$  is unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or  
 15 mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl ester, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl sulfone or unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl nitrile with the  
 20 sulfinimine derivative of the compound of formula ( $\alpha$ ) to yield a desoxy - amine - hydrocarbyl derivative of the compound of formula ( $\alpha$ ); or

(ivc) reacting an nitro alkyl reagent of formula



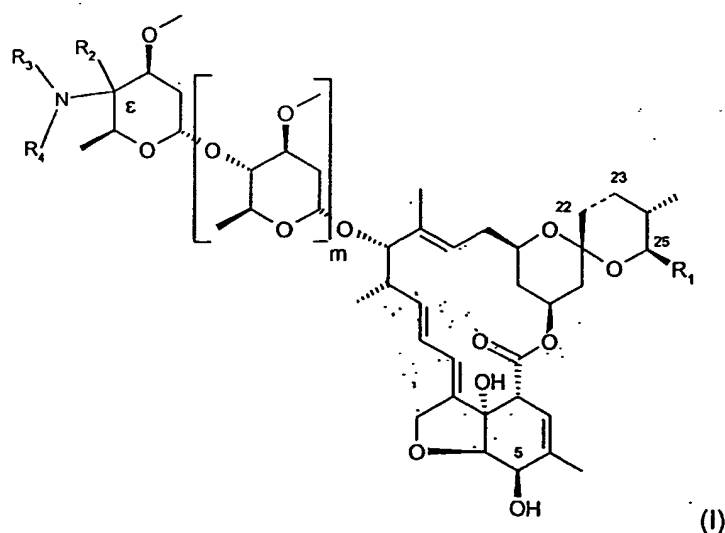
where  $R_{10}$  and  $R_{11}$  are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl,  
 25 unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to

- pentasubstituted C<sub>2</sub>-C<sub>12</sub>alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl sulfone or
- 5 unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy - amine - hydrocarbyl derivative of the compound of formula (α); and

either

- (va) removing the sulfinyl group and protecting group Q either in one step or sequentially
- 10 one after another to yield a compound of formula (I), where R<sub>3</sub> and R<sub>4</sub> each represent hydrogen, or
- (vb) removing the sulfinyl group alone, carrying out reactions on one or more of the R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> groups to modify the group and then removing the protecting group Q to yield a compound of formula (I), or
- 15 (vc) removing the protecting group Q if the sulfinyl group is removed during (iva) or (ivb) or (ivc) to yield a compound of formula (I).

3. A process for preparing a compound of formula (I)

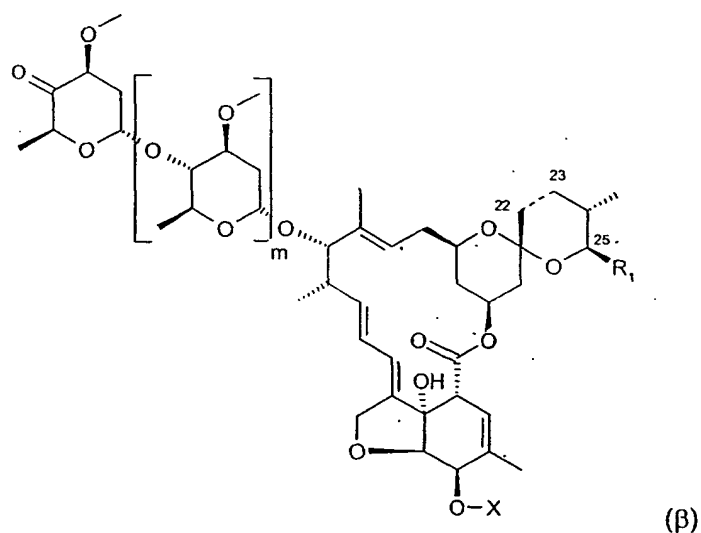


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wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined in claim 1, comprising the steps of:

5

(i) synthesizing a compound of formula ( $\beta$ )



wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  is as defined for formula (I) in claim 1 and  $X$  is H or Q, where Q is a protecting group;

10

(ii) reacting N- $R_4$ hydroxylamine or salt thereof with a compound of formula ( $\beta$ ) to yield a nitron derivative of the compound of formula ( $\beta$ );

either

15 (iia) reacting an organometallic or a silyl reagent having the  $R_2$  group with nitron derivative of the compound of formula ( $\beta$ ) to yield a desoxy - N- $R_4$ hydroxylamino - hydrocarbyl

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derivative of the compound of formula (β), where R<sub>4</sub> is as defined for formula (I) in claim 1,  
or

(iiib) reacting an alkene or an alkyne derivative with the nitron derivative of the compound  
of formula (β) to yield a desoxy – N-isoxazolidine derivative or 2,3-dihydro-isoxazole

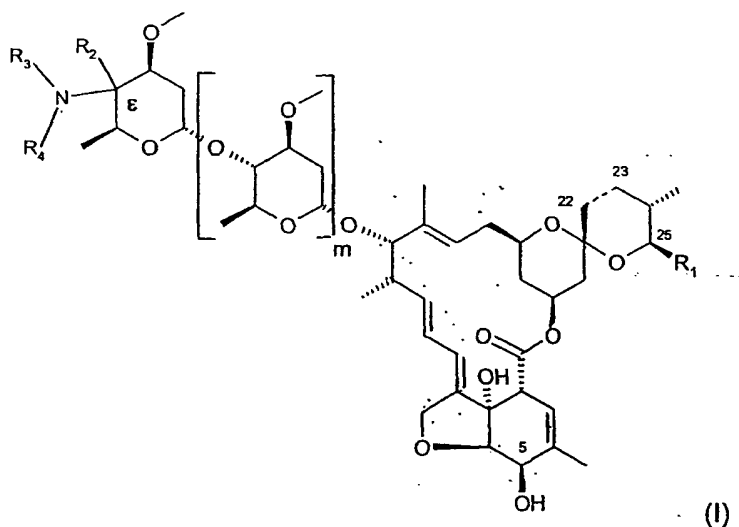
5 derivative respectively of the compound of formula (β); and

either

(iva) removing the protecting group Q, if present, to yield a compound of formula (I), where  
R<sub>3</sub> is OH in the event of reaction step (iiia), or where R<sub>2</sub> and R<sub>3</sub> is an alkylene or alkenylene  
10 bridge with a CH<sub>2</sub> group replaced by an oxygen atom in the event of reaction step (iiib), or

(ivb) carrying out reactions on one or more of R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> groups to modify the group and  
removing the protecting group Q, if present, to yield a compound of formula (I).

4. A process for preparing a compound of formula (I)

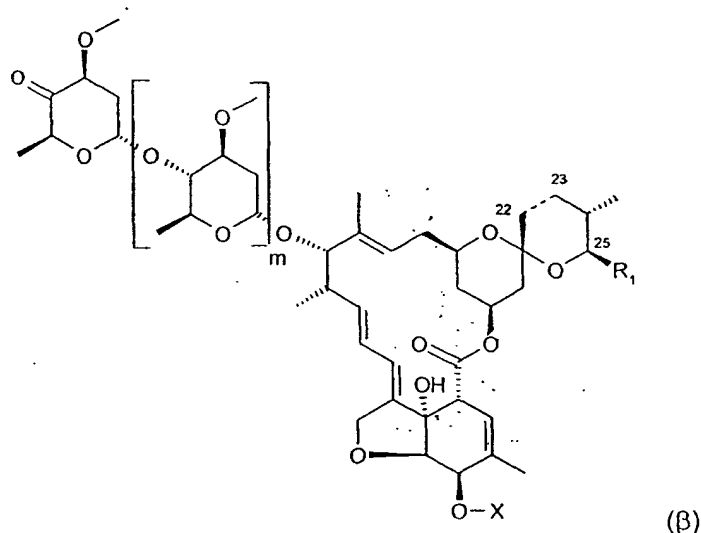


15

wherein R<sub>1</sub>, R<sub>3</sub>, R<sub>4</sub>, the bond between the carbon atoms 22 and 23 and m are as defined in  
claim 1 and R<sub>2</sub> is CN, comprising the steps of:



(i) synthesizing a compound of formula ( $\beta$ )



wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  is as defined in for  
 5 formula (I) in claim 1 and X is H or Q, where Q is a protecting group;

either

(iia) reacting the compound of formula ( $\beta$ ) with a silylated amine (having the  $R_3$  and  $R_4$   
 groups) in presence of a Lewis acid and a trialkylsilyl cyanide, to yield a compound of  
 10 formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q  
 is present, and wherein  $R_1$ ,  $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and  $m$   
 are as defined in claim 1, and  $R_2$  is CN, or

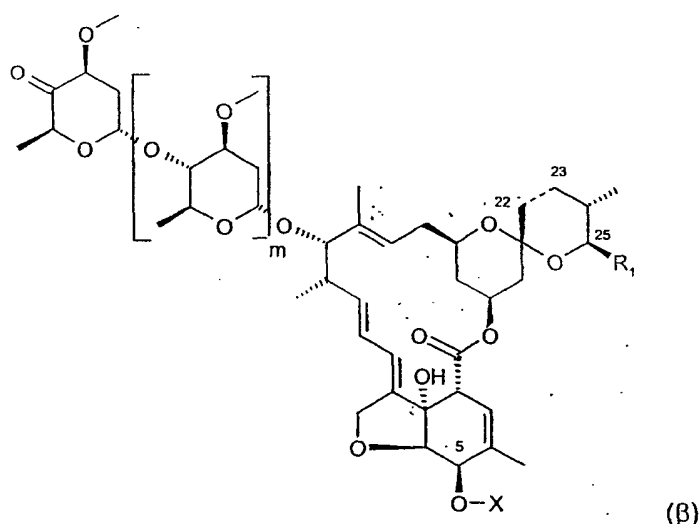
(iib) reacting the compound of formula ( $\beta$ ) with an amine of formula  $R_3R_4NH$ , a chlorosilane,  
 a Lewis acid and a trialkylsilyl cyanide to yield a compound of formula (I) with the proviso  
 15 that the oxygen atom at the 5-carbon position is protected, if Q is present, and wherein  $R_1$ ,  
 $R_3$ ,  $R_4$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined in claim 1, and  
 $R_2$  is CN;

(iii) optionally carrying out reactions on one or both of  $R_3$  and  $R_4$  groups to modify the group; and

(iv) removing the protecting group Q, if present, to yield a compound of formula (I);

5 or

(i) synthesizing a compound of formula ( $\beta$ )



wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined for formula (I) in claim 1 and  $X$  is H or Q, where Q is a protecting group;

10

(ii) reacting the compound of formula ( $\beta$ ) with an ammonium salt of formula  $R_{18}CO_2NH_4^+$ , an isocyanide of formula  $R_{12}NC$  to yield a compound of formula (I), with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula ( $\beta$ ), wherein  $R_1$ , the bond between the carbon atoms 22 and 23 and  $m$  are as defined in claim 1,  $R_2$  is  $R_{12}NHC(O)$ , and  $R_4$  is  $R_{18}C(O)$ ,  $R_{18}$  is H, unsubstituted or mono- to pentasubstituted  $C_1$ - $C_{12}$ alkyl, unsubstituted or mono- to pentasubstituted  $C_3$ - $C_{12}$ cycloalkyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkenyl, unsubstituted or mono- to pentasubstituted  $C_2$ - $C_{12}$ alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to

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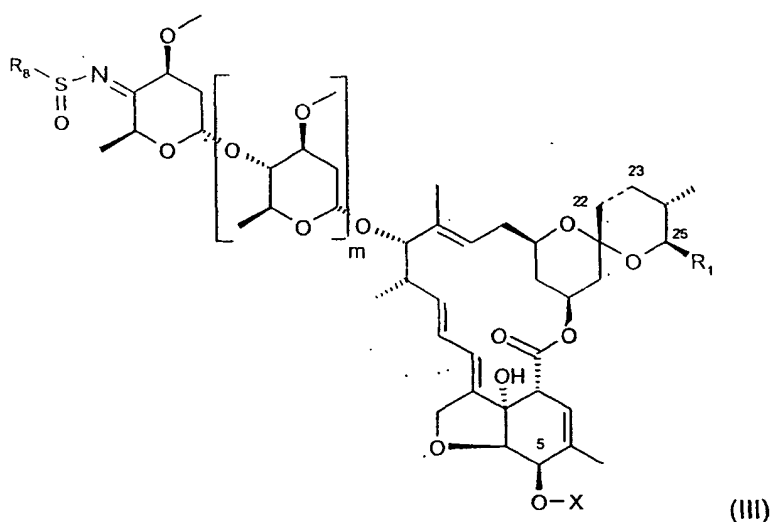
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pentasubstituted C<sub>3</sub>-C<sub>12</sub>cycloalkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl ester, unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl sulfone or unsubstituted or mono- to pentasubstituted C<sub>1</sub>-C<sub>12</sub>alkyl nitrile and R<sub>12</sub> is as defined in claim 2; and

5

(iii) removing the protecting group Q, if present, to yield a compound of formula (I).

5. A compound of the formula (III)



wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

10

m is 0 or 1,

R<sub>1</sub> represents a C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl, group,

R<sub>8</sub> represents C<sub>1</sub>-C<sub>6</sub>alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C<sub>1</sub>-C<sub>6</sub>alkoxy, hydroxy, cyano, aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO<sub>2</sub>, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>1</sub>-C<sub>12</sub>haloalkyl, C<sub>1</sub>-C<sub>12</sub>alkoxy, C<sub>1</sub>-C<sub>12</sub>haloalkoxy, C<sub>1</sub>-C<sub>12</sub>alkylthio and C<sub>1</sub>-C<sub>12</sub>haloalkylthio, and

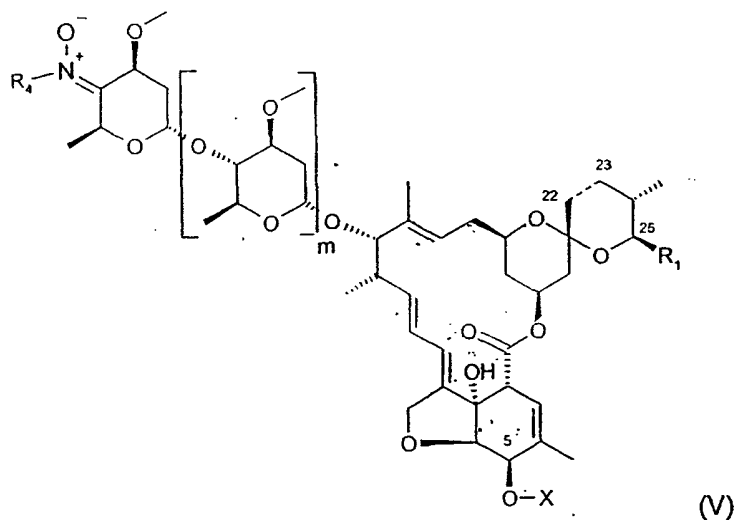
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X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position;

or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (III), in each case in free form or in salt form.

5

6. A compound of the formula (V)



wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

10 m is 0 or 1,

R<sub>1</sub> represents a C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl, group,

R<sub>4</sub> represents a chemical constituent, and

X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (V), in each case in free form or in salt form.

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7. A pesticidal composition comprising at least one compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively, as active compound, and at least one auxiliary.
- 5 8. A method for controlling pests comprising applying a composition defined claim 7 to the pests or their habitat.
9. A process for preparing a composition defined in claim 7 comprising mixing intimately and/ or grinding at least one compound least one compound of the formula (I), (III) or (V),  
10 as defined in claim 1, 5 or 6 respectively, as active compound, with at least one auxiliary.
10. The use of a compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively, for preparing a composition as defined in claim 7.
- 15 11. The use of a composition as defined in claim 7 for controlling pests.
12. A method for protecting plant propagation material comprising treating the propagation material, or the location where the propagation material is planted, with a composition defined in claim 7.
- 20
13. A pest resistant plant propagation material having adhered thereto at least one compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively; preferably treated by the method of claim 12.
- 25 14. The use of compound defined in claim 5 or 6 for preparing a compound of formula (I) as defined in claim 1.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2005/002489

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07H19/01 A01N43/90 A61K31/7048 A61P33/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07H A01N A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, CHEM ABS Data		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 375 393 A (MERCK & CO. INC) 27 June 1990 (1990-06-27) -----	
A	WO 93/15099 A (PFIZER LIMITED; PFIZER INC) 5 August 1993 (1993-08-05) -----	
A	EP 0 343 708 A (MERCK & CO. INC) 29 November 1989 (1989-11-29) cited in the application -----	
<div style="display: flex; justify-content: space-between;"> <span><input type="checkbox"/> Further documents are listed in the continuation of box C.</span> <span><input checked="" type="checkbox"/> Patent family members are listed in annex.</span> </div>		
<div style="display: flex;"> <div style="flex: 1;"> <p>* Special categories of cited documents:</p> <p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="flex: 1;"> <p>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>*G* document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search  <div style="text-align: center; font-weight: bold;">24 June 2005</div>		Date of mailing of the international search report  <div style="text-align: center; font-weight: bold;">01/07/2005</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  <div style="text-align: center; font-weight: bold;">Bardili, W</div>

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